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A SYSTEM OF PRACTICAL MEDICINE

BY

AMERICAN AUTHORS.

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VOLUME I.

INFECTIOUS DISEASES.

ILLUSTRATED.

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PREFACE TO VOLUME I.

RECENT years have been characterized by fruitful investigation of the causes of disease, and by the increasing definiteness of modern medicine in its practical applications.

Such considerations render obvious the necessity for a systematic and practical work covering the entire field of general and special medicine in its foremost state of development. To meet this want the late Dr. Alfred Lee Loomis, LL.D., undertook the editorship of the SYSTEM OF PRACTICAL MEDICINE BY AMERICAN AUTHORS, and associated me with himself in its charge. His eminent standing brought the willing co-operation of leading American practitioners and teachers, and it has thus been possible to assign each subject to an author of the highest repute in its special branch. It is therefore not unreasonable to anticipate that these volumes will be accepted as representative and as satisfying practical needs, and that they will do credit to the fair name of America in the world of medicine.

While ample space is allotted for all that the physician can care to know of practical medicine, matters historical and purely controversial have been omitted. No general articles upon hygiene, bacteriology, or symptomatology have been introduced, all necessary knowledge of such character being included in the special articles upon the various diseases—an arrangement affording the advantage of making each subject complete in itself. The greater specialties lying out of the domain of general medicine have likewise been omitted, as readers can more usefully consult the many excellent treatises on gynæcology, ophthalmology, dermatology, etc.

It has thus been found possible to present a succinct and complete account of medical practice in its latest aspects, each article being a clinical monograph and proceeding from the cause and nature of a disease to its diagnosis, prognosis, and treatment. The therapeutical sections have been made especially rich and precise, since, after all, the main object of medical science is curative. Prescriptions and formulæ will be found wherever they can be of assistance. Diagrams, charts, and tables have been frequently employed, in view of the clearness and vividness of knowledge which can be imparted by such means, and illustrations and colored plates have not been spared where they could serve utility. Most of these illustrations will derive an added interest from their originality, prepared, as they have been, especially for this work. Careful study has been bestowed upon the typographical arrangement and sub-headings of the various articles, and a system has been followed which will facilitate consultation. Much care has been given to the indexes, as upon their completeness depends very greatly the convenience and utility of the entire work. Each volume will be separately indexed. Due credit has been awarded in the text and foot-notes for important discoveries in medicine.

A closing word is due and affectionately rendered to Professor Loomis. He secured the authors, apportioned their subjects, decided the arrangement and classification of the entire work, and discussed with me many important details, so that in completing the editorial duties alone I have been able to carry out the designs which he had already formulated. He was one of the world's great masters of medicine; he leaves it richer for this result of his knowledge of the science and of his contemporaries who could fitly join him in expounding it. His own article on Endocarditis will be read with all the interest attaching to the latest production of a man universally admired for his attainments and respected for his personality.

To the eminent clinicians and teachers who share in the authorship of these volumes I desire to extend thanks for their uniform courtesy and assistance in the execution of an editorial task necessarily large and difficult.

W. GILMAN THOMPSON, M. D.

NEW YORK, January, 1897.

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MALARIA.

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DEFINITION, SYNONYMS, HISTORY, AND PARASITOLOGY.

BY WILLIAM H. WELCH, M. D.

DEFINITION.

MALARIA comprises the diseases caused by the specific protozoan parasite called *Hæmatozoön malariæ.*

The name "malaria," derived from the Italian *mal' aria* and signifying "bad air," was applied originally to the miasm or poison which was supposed to produce the disease. It is now used to designate the disease itself, and is the most convenient term for this purpose.

The most characteristic malarial manifestations are intermittent or remittent fever, certain forms of the disease described as "pernicious," and a chronic cachexia with enlarged spleen and anæmia. The parasite discovered by Laveran is invariably present in malaria and produces from the hæmoglobin of the red blood-corpuscles the brown or black pigment granules which are characteristic of the disease.

SYNONYMS.

Malarial fever; Intermittent fever; Chills and Fever; Fever and Ague; Paludism or Paludal fever; Swamp or Marsh fever; Miasmatic fever; Periodical fever; Autumnal fever.

Names derived from localities where the disease has prevailed with especial intensity have sometimes been used; as, Walcheren fever, Batavia fever, Hungarian fever, African fever, Panama fever, Chagres fever.

Special names have been applied to certain types or manifestations of malaria; as, remittent fever, bilious remittent fever, hemorrhagic remittent fever, congestive fever, dumb ague, black-water fever, black jaundice.

HISTORY.

There are few diseases which can be traced so surely and continuously as malaria in medical writings from ancient times to the present. Various types of malarial fever are described by Hippocrates, Celsus, Galen, and other ancient writers, although it is often impossible to determine the precise characters of many of the fevers described by these authors.

Celsus and Galen divide intermittent fevers into quotidian, tertian, quartan, semi-tertian, and irregular. They recognized intermittent fevers with long intervals. The nature of their semi-tertian fever (hemitritæus) has given rise to much discussion. Certain forms of intermittent fever were believed by Galen to have their seat in the spleen, others in the liver. The influence of marsh effluvia and of seasons of the year in the causation of certain of these fevers was recognized. Various symptoms were discriminated as to their prognostic significance, often with much acuteness of observation. A passage in Celsus clearly alludes to the type of malarial fever now called æstivo-autumnal fever.

The Arabian physician Rhazes described the so-called subintrant malarial fevers. No important advance beyond the knowledge of Celsus and of Galen concerning malarial fevers was made until toward the end of the sixteenth century, when Mercatus in his work on malignant fevers described various forms of pernicious paroxysms in association with intermittent fever, particularly with the tertian type.

The introduction of cinchona bark from Peru into Europe by the Countess del Chinchon and her body-physician, Juan del Vego, in 1640, gave great impetus to the study of malarial fevers, and, indeed, in its revolutionizing influence upon medical doctrines this event marks an epoch in the history of medicine.

In the latter half of the seventeenth and the beginning of the eighteenth century there appeared a voluminous literature regarding malarial fevers. The most notable of the works upon this subject of this period are those of Sydenham, Richard Morton, Torti, Ramazzini, and Lancisi. These works remain to this day the great classics upon malaria. They contain the fundamental clinical and therapeutical facts and many etiological data relating to this disease. Morton and Lancisi demonstrated clearly the relation of malaria to marsh miasm. Sydenham pointed out the differences between vernal and autumnal intermittent fevers. Especially complete and keen in analysis is the nosography of Torti,[1] whose classification of the malarial fevers, particularly of the pernicious and mixed forms, has been followed by most subsequent authors. The diagnostic as well as the therapeutic value of the preparations of Peruvian bark was recognized, and assisted materially in the discrimination of the malarial fevers from the other so-called essential fevers. It is interesting to note the relative accuracy of diagnosis and of description of the group of malarial fevers from the latter half of the seventeenth century onward, in contrast to the confusion which existed regarding the other essential fevers until the discrimination of the latter by the pathological-anatomical studies of the present century.

The military and colonial enterprises of England in the eighteenth century served to extend the knowledge of the geographical distribution of malaria, particularly in tropical climates, the works of Pringle and of Lind containing especially noteworthy observations on this point. But the great mass of the very extensive literature on the epidemiography of malarial diseases which has been so industriously collected and ably analyzed by Hirsch[2] belongs to the present century.

---

[1] Torti: *Therapeutice specialis ad febres quasdam perniciosas, etc.*, Mutinæ, 1712.

[2] Hirsch: *Handbuch der historisch-geographischen Pathologie*, Stuttgart, 1881.

The significance, as regards malaria, of the active studies in morbid anatomy of the first half of the present century relates to the clear differentiation of typhoid fever from malarial and other fevers rather than to the actual contributions to the pathology of malaria, although these were not lacking. The occurrence of enlarged spleens, so-called fever-cakes or ague-cakes, and even the dark color of the organs in association with malarial fevers, had been occasionally observed by the older writers, notably by Lancisi, but the intimate relation of these alterations to malaria was not established until during the first half of the present century.

Audouard (1808, 1812, 1818) emphasized congestion and enlargement of the spleen as the essential anatomical lesion of malarial fever. Bailly (1825) noted in a series of autopsies on cases of pernicious malarial fever observed in Rome in 1822 the dark color of the cortical gray matter of the brain and the congestion of the cerebral meninges and substance. He laid especial emphasis upon evidences of supposed inflammation of the central nervous system and of the stomach and intestine. These anatomical observations, together with those of Nepple (1828, 1835), and, to a less extent, of Maillot (1835), were interpreted in favor of Broussaisism, which at this period exerted such a pernicious influence upon medical practice.

Valuable contributions to the pathological anatomy of malarial fevers, especially of the remittent type, were made in the United States during the fourth decade of this century by Stewardson in Philadelphia, Swett in New York, and Anderson and Frick in Baltimore. Stewardson demonstrated the bronzed color of the liver in remittent fevers, and regarded this as the characteristic anatomical criterion of the disease. His observations were confirmed and extended by the other writers named. Alonzo Clark in 1855 demonstrated that the bronzed color of these livers is due to the presence of granules of yellow, brown, and black pigment, which he regarded as derived from the coloring matter of red blood-corpuscles. The monumental work of Daniel Drake on *The Principal Diseases of the Interior Valley of North America* (1850, 1854) contains a large amount of valuable information, based upon personal observation and research, as to the distribution and characters of the malarial fevers in the then Western States of this country.

In the light of recent discoveries it is interesting to note the ingenious arguments advanced by John K. Mitchell in his work *On the Cryptogamous Origin of Malarious and Epidemic Fevers*, published in 1849, in favor of the doctrine of contagium animatum. This book deserves to rank with the more frequently quoted work of Henle relating to the same line of argument. At about the same period Bassi and Rasori in Italy also advocated the parasitic theory of malaria.

The discoverer of the malarial pigment is Heinrich Meckel, who found and described the pigment in 1848 in the blood and organs of the dead body of an insane patient. He was, however, ignorant of the relation of this pigment to malaria. The next report concerning the pigment was in 1849 by Virchow, who observed it in the body of a man who had suffered from chronic malaria. There soon followed the observations of Heschl, Planer, A. Clark, Tigri, Frerichs, and others, fully establishing the relation of the pigment to malaria. The source of the pigment was regarded by Meckel and Virchow as in the spleen, and this doctrine was elaborated by Frerichs. Planer (1854) was the first who saw the pigment in the fresh blood of living patients, and he suggested that the pigment may be formed in the circulating blood—a view which was more fully presented and advocated by Arnstein (1874) and by Kelsch (1875).

There is no doubt that some of the pigmented bodies which are now recognized as parasitic organisms had been seen by earlier observers without knowledge of their true nature. Thus Meckel noted the presence of pigment granules in colorless, hyaline bodies devoid of definite nuclei. He, and more particularly Virchow and Frerichs, observed pigment in fusiform and curved bodies in the blood, which, although interpreted as endothelial cells of splenic origin, in all probability were, at least in part, the crescentic forms of the parasite. Some of the larger pigmented spherical organisms must have been seen and mistaken for pigmented leucocytes.

In November, 1880, Laveran discovered the parasitic nature of these and previously unrecognized forms in the blood of malarial patients, and thereby introduced a new era into our knowledge of the malarial diseases.

The discovery of the malarial parasite has furnished an unfailing means of diagnosis of malarial diseases, has materially advanced our knowledge of their pathology, has led to a better understanding of their clinical phenomena and various types, has furnished important data for prognosis, and has led to improvements in methods of treatment.[1]

PARASITOLOGY.

HISTORICAL.

In 1879, A. Laveran, a French military surgeon, stationed at the time in the province of Constantine, Algeria, began to study the pathological anatomy of malaria, and at once directed his attention to the much discussed question of the origin of the pigment. He observed in the blood of malarial patients certain pigmented bodies different from the melaniferous leucocytes, but he was uncertain as to their nature until, on November 6, 1880, he discovered that some of these pigmented bodies threw out long flagella endowed with such active lashing movements as to convince him, as they have convinced every one who has since then seen them, that they are living parasites. Laveran published his observations in a note to the Académie de Médecine in Paris, presented November 23, 1880. This was followed by the publication of several notes in 1880 and 1881, and in the latter year appeared a small monograph by Laveran on the parasitic nature of malaria.[2]

---

[1] The so-called bacillus malariæ described in 1879 by Klebs and Tommasi-Crudeli, which for a short period had a certain vogue, chiefly with Italian writers, never rested upon satisfactory observations which indicated that it bore any relation to malaria, and it deserves no more consideration than the palmella of Salisbury and the other alleged malarial organisms described before Laveran's discovery.

[2] Only occasional references to the voluminous literature on the parasitology of malaria are given in this article. A full table of references to the works treating of malarial fever since the recognition of its parasitic origin up to and partly including the year 1895 will be found in "The Malarial Fevers of Baltimore," by William Sydney Thayer, M. D., and John Hewetson, M. D. (*The Johns Hopkins Hospital Reports*, vol. v., 1895).

In these various early publications Laveran describes (1) pigmented crescentic and ovoid bodies; (2) spherical, transparent bodies, sometimes free, sometimes applied to the surface of red blood-corpuscles, the smallest about one-sixth of the diameter of a red blood-corpuscle and containing only one or two fine pigment granules, these representing an early stage of development of (3) larger, pigmented, spherical bodies averaging 6 μ in diameter, but sometimes larger than a red blood-corpuscle, and containing numerous, often moving, pigment granules; (4) bodies similar to the last mentioned, but beset with actively motile flagella; (5) free motile flagella; and (6) swollen spherical or deformed bodies, 8–10 μ in diameter, containing pigment, and regarded as cadaveric forms of the spherical parasites. Laveran noted amœboid movements of the spherical forms, grouping of the small spherical bodies together, and the occurrence of small, colorless, motile bodies, without specific characters, which he suggested may perhaps represent the first phase of development of the parasitic elements. He regarded all of the forms as different stages of development of the same species of organism, and considered the free flagella, which he believed were formed within the spherical bodies and escaped by rupture of the enveloping membrane, as the most characteristic and perfect stage of development of the parasite.

Laveran communicated his results to his colleague Richard, stationed in Philippeville, Algiers, who in February, 1882, published a communication confirming Laveran's observations and adding certain points of importance. He describes the development of the parasite from small, perfectly transparent bodies contained in otherwise normal red blood-corpuscles. This clear body grows larger, forms pigment out of the hæmoglobin of the enveloping red corpuscle, which thereby becomes gradually decolorized and reduced to a mere colorless shell-like rim, which finally ruptures and sets free the parasite. This now generally accepted view as to the intracorpuscular development of the parasite, which was first announced by Richard, was, however, in the following year abandoned by him in favor of Laveran's view that the parasites develop either free in the plasma or in close attachment to the surface of red corpuscles or in depressed spots on the surface. Richard observed amœboid movements of the parasites, and noted spherical bodies with a central block of black pigment from which delicate lines radiated so as to produce rosette forms.

Laveran continued to publish brief communications in 1882 and 1883, and in 1884 he published a larger work[1] presenting his observations and views in detail. In this work he describes more fully the forms already mentioned, and he notes the occurrence of segmenting forms, which, however, he interpreted as forms of degeneration, not of reproduction.

The observations of Laveran and of Richard were made by microscopical examination of the fresh blood. In 1883 and 1884, Marchiafava and Celli published in a number of articles the results of their studies of stained specimens of dried malarial blood. With the exception of small, spherical stained bodies in the red blood-corpuscles, which they thought might be micrococci, they interpreted the various other stained and usually pigmented bodies found in the red corpuscles of malarial patients as probably degenerative changes. As a matter of fact, the coccus-like dots were probably in part Ehrlich's degenerations, whereas their drawings show that the supposed degenerative forms were in reality the actual parasites, which in many of their phases were accurately depicted, although not recognized as such.

---

[1] Laveran : *Traité des Fièvres palustres*, Paris, 1884.

In 1885, Councilman and Abbott in the organs from two cases of pernicious comatose fever found and described small pigmented hyaline bodies in and outside of red corpuscles, most abundantly in capillaries of the brain.

In 1885, Marchiafava and Celli, as the result of the examination of fresh malarial blood, came to a correct interpretation of these bodies and described them fully and accurately. They emphasized especially the amœboid, unpigmented, transparent intracorpuscular bodies, to which they gave the inaccurate name of plasmodia, which has been widely adopted. They described clearly the intracorpuscular development of the parasite, the formation of pigment out of the blood coloring matter, the consequent changes in the blood-corpuscles, and they pointed out the probable reproductive nature of the segmenting bodies, which they described more fully and accurately than had been done by Laveran and Richard.[1]

The publications of Marchiafava and Celli attracted wider attention than had those of Laveran, and from the year 1885 up to the present time there has been a steadily flowing stream of literature upon the various questions connected with the parasitology of malaria.

Immediately following the confirmation of Laveran's discoveries by Italian observers came similar confirmation from Sternberg, Councilman, and Osler (1886–87), and somewhat later by James (1888) and Dock (1890), in this country, and within a few years numerous reports from various parts of Europe, America, Asia, and Africa demonstrated the invariable association of Laveran's parasites with all cases of malarial fever. There are no observers of any prominence who, with sufficient opportunity and training for such examinations, have failed to recognize the parasites in cases of malaria, nor is there now any authoritative voice of dissent from the acceptance of the parasite as the specific cause of this disease.

Since the fundamental researches of Laveran, Richard, and Marchiafava and Celli (1880–85) other observers have greatly extended our knowledge as to many details concerning the structure and life-history of the parasite and its relation to various types, phenomena, and lesions of malaria, although not a few important questions still remain unsettled. The most important of these later discoveries are due to the demonstration by Golgi (1885–86) of a definite relation between the cycle of development of the parasite and the different stages of malarial fever, and to the recognition by Golgi (1885–86) of the two varieties of the parasite belonging respectively to quartan and to tertian fever, and by Marchiafava and Celli and Canalis (1889) of the variety or varieties belonging to æstivo-autumnal fever. These observations have led to two schools of doctrine—the one, headed by Laveran, holding to the unity of a pleomorphic malarial parasite, the other, headed by Golgi and other Italian writers, upholding the plurality of malarial parasites. The latter doctrine has the larger number of supporters.

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[1] Marchiafava and Celli claim for themselves the discovery of the intracorpuscular amœboid forms with and without pigment, and of the segmenting forms, but, as is apparent from the review of Laveran's and Richard's preceding publications, this claim cannot be admitted. Marchiafava and Celli, however, described and interpreted these phases of the parasite far better than Laveran, and to them belongs the credit of demonstrating the intracorpuscular development of the parasite.

Dock (1890–92) was the first to differentiate the three principal varieties of the malarial parasite in the United States, and recently Thayer and Hewetson[1] have published a thorough study of the malarial fevers of Baltimore with careful descriptions of these varieties.

Investigations concerning the intimate structure of the malarial parasites have been made especially by Celli and Guarnieri, Grassi and Feletti, Romanowsky, Sacharoff, Mannaberg, Antolisei, Bastianelli and Bignami, and others.

The results of these later studies concerning the malarial parasites will be considered in various parts of this article. They are fully and systematically presented in the recent monograph of Thayer and Hewetson, already cited.

NOMENCLATURE.

Various names have been suggested for the malarial parasite. Among these may be mentioned Oscillaria malariæ (Laveran), Plasmodium malariæ (Marchiafava and Celli), Hæmatomonas malariæ (Osler), Hæmatophyllum malariæ (Metchnikoff), Hæmamœba malariæ (Grassi and Feletti), Hæmococcidium malariæ (L. Pfeiffer), Hæmosporidium malariæ (Danilewsky), Hæmatozoön or Hæmocytozoön malariæ (Osler and various authors).

Of these names, Plasmodium malariæ has gained wide currency, but it is on zoölogical grounds singularly inappropriate, and there is no reason why it should be perpetuated.

The name Hæmosporidium malariæ has much to recommend it, but it has not been generally adopted. Upon the whole, the name Hæmatozoön malariæ, which expresses nothing as to the zoölogical classification of the parasite, and which has been adopted by many writers, may be provisionally accepted until more precise knowledge is reached concerning the zoölogical position of the parasite. Hæmocytozoön is more precise, but the other term has the advantage of greater brevity.

ZOÖLOGICAL POSITION OF THE MALARIAL PARASITE.

The malarial parasite belongs to the class of Protozoa, under which name are grouped the unicellular organisms with the physiological characters of animals. Bütschli divides the Protozoa into the orders—Sarcodina, Mastigophora, Sporozoa, and Infusoria. Grassi and Feletti classify the malarial parasite among the Sarcodina, subdivision Rhizopoda, and adopt the name Hæmamœba malariæ. Antolisei considers that the parasite belongs to the Gymnomyxa, or, more precisely, the Proteomyxa of Ray Lankester. The great majority of authors classify the malarial parasite among the Sporozoa, which are divided by Balbiani into the groups Gregarinida, Sarcosporidia, Myxosporidia, and Microsporidia. Under the Gregarinidæ are included the Coccidia, with which some writers group the malarial parasite. Kruse makes under the Gregarinidæ a special family which he designates as Hæmogregarinidæ, and to which he refers the malarial parasite and similar hæmocytozoa in lower animals. Danilewsky suggests forming a new group under the Sporozoa to be called Hæmosporidia, in which he places the malarial and similar hæmatozoa, and Labbé calls the group Gymnosporidia.

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[1] *Op. cit.*

As we know nothing of the malarial parasite in the outer world, it is evident that our knowledge of its life-history is incomplete, so that any attempt at a zoölogical classification must be regarded as only provisional. Such information as we possess favors classifying the parasite among the Sporozoa, but it possesses characters which do not enable us to fit it exactly into any of the existing subdivisions of the Sporozoa, so that the suggestions of Kruse and of Danilewsky of establishing a new subdivision of the Sporozoa or of the Gregarinidæ to include the malarial parasite and similar organisms in birds seems to be a good one, and the name Hæmosporidia for this new subdivision appears to be appropriate. According to this classification, the malarial parasite may be called the Hæmosporidium malariæ.

METHODS OF INVESTIGATION.

The methods for demonstrating and studying the malarial parasite will be described under the heading *Diagnosis*. It may here be stated that generally the most useful procedure is the examination of thin layers of fresh blood with an oil-immersion objective. The description of the parasite which is to follow is based mainly upon this method. This procedure may be advantageously combined with the examination of stained specimens. For the study of the finer details of structure this latter method is indispensable.

GENERAL MORPHOLOGY AND BIOLOGY.

The malarial parasite is a unicellular, protozoan organism which develops within the red blood-corpuscles, and therefore belongs to the group of Hæmocytozoa. As will be described subsequently, organisms closely resembling the malarial parasite have been found in the blood of birds. The numerous attempts to cultivate artificially the malarial parasite have hitherto been unsuccessful, nor has this organism been recognized in the outer world. Our entire knowledge of it is derived from its study in human beings.

Three varieties of the parasite have been differentiated. These varieties are that of quartan fever, that of tertian fever, and that of æstivo-autumnal fever. This last variety it is proposed by the writer to call the Hæmatozoön malariæ falciparum. Before considering the justification of this division and the special characters of each of these varieties it is desirable to describe the more important characters common to all varieties of the malarial parasite.

The cycle of development of the malarial parasite embraces a vegetative and a reproductive phase. Its duration varies from twenty-four to seventy-two hours, according to the variety of parasite.

The vegetative phase begins in the form of small, colorless, amœboid, hyaline bodies, 1–2 μ in diameter, within the red blood-corpuscles.[1] These amœboid bodies increase in size, and, with the occasional exception of the æstivo-autumnal variety, they develop within them a variable number of dark pigment-granules, situated, as a rule, near the margin of the parasite. The pigment increases in amount and in the coarseness of the granules as the organisms continue to develop. It occurs in the form of irregular grains and of fine rods, which may be in active motion within the parasite.

Having attained a certain stage of development, which differs as regards the size of the organism in the different varieties, the parasite gradually ceases its amœboid movements, assumes a spherical or oval shape, and becomes somewhat sharper in contour. In this condition it may continue for a while to grow. When it has reached its full size it may completely fill the red blood-corpuscle or may occupy only a small part of it, these differences depending mainly upon the variety of parasite. The parasite now may be called the full-grown or adult form.

Coincidently with these stages of development the enveloping red blood-corpuscle may undergo various changes, which are of significance in distinguishing the varieties of parasite from each other. The corpuscle may become swollen and pale, or shrunken, or brassy-green in color, or otherwise deformed, or it may appear unaltered, as will be described in considering the varieties of the parasite.

The subsequent stages in this cycle of development belong to the reproductive phase, which is shorter in duration than the vegetative. The first evidence of this reproductive phase is the collection of the pigment into a mass of granules or a solid block situated usually at or near the centre, but sometimes near the periphery, of the organism. These bodies with clumps of pigment may be designated, in accordance with Thayer and Hewetson's suggestion, as the presegmenting forms (*corpi con blocchetto* of the Italian writers).

Coincidently with or following this gathering of the pigment into a clump, sometimes without a definite collection of the pigment, the process of segmentation begins. In its most typical form segmentation is ushered in by the appearance of delicate lines radiating from the periphery toward the centre. Eventually the substance of the spherical organism is divided into a variable number of round or oval bodies called spores. The enveloping red corpuscle, which now may be

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[1] As has already been mentioned, Laveran believes that the forms of the parasite which have, since the publications of Marchiafava and Celli, usually been regarded as within the red corpuscles, are attached or applied (*accolés*) to the outer surface of the corpuscles. Mannaberg (1893) has again raised this question by his statement that many of the amœboid forms, particularly in their younger stages of development, are attached to the corpuscles, often in little niches or indentations on the surface. There is no doubt that the organism may be situated as described by Mannaberg. Marchiafava and Celli, who had previously noted this appearance, interpreted it as indicating the extrusion of the parasite from the red blood-corpuscle. It is, in fact, often very difficult to determine with precision whether the organism is on the surface of or within the corpuscle, but the evidence is that the majority of the younger forms are intracorpuscular. Marchiafava and Bignami (1894) describe in the following words their conception of the manner of penetration of the youngest forms into the corpuscle: "The youngest amœbæ, the offspring of sporulation, by virtue of the viscidity of their protoplasm adhere to the surface of, and by their movements bury themselves in, the contour of the red corpuscle. In this position the parasite attacks the external strata of the corpuscle as a means of nourishment, and after altering these layers is able to penetrate within, and thus becomes entirely endoglobular."

reduced to a narrow pale rim, bursts and the spores are set free, or the corpuscle may have disappeared before the process of segmentation is completed. The pigment remains behind, and is quickly engulfed by phagocytes. Sometimes in the æstivo-autumnal variety segmentation occurs in organisms entirely devoid of pigment. These segmenting bodies are called also sporulating forms.

The free spores speedily invade fresh red blood-corpuscles, where, as the small, colorless, amœboid, hyaline bodies already mentioned, they begin again the cycle of development. The direct transformation of the motionless[1] round spores into the small, hyaline, amœboid bodies has been very rarely observed, but there is no reason to suppose that there exists any stage intervening between these two forms.

In the complete sporulating cycle of development which has been described we can distinguish, therefore, the following forms of the parasite: (1) unpigmented, amœboid, hyaline bodies; (2) pigmented, amœboid, hyaline bodies; (3) full-grown or adult bodies; (4) presegmenting bodies; (5) segmenting or sporulating bodies; and (6) spores. All of these various bodies are depicted in Plates I. and II.

As already mentioned, in the æstivo-autumnal variety this cycle may be completed without the appearance of pigment. These bodies are to be thought of, not as separate and distinct forms, but simply as successive stages of development with all transitions from the youngest to the most advanced. Especially can no sharp distinction be drawn between bodies (1) and (2) and between bodies (3) and (4). The recognition, as a distinct form, of the body designated as presegmenting is of less practical importance for the quartan and tertian varieties than for the æstivo-autumnal.

The name "plasmodium" was applied by Marchiafava and Celli originally to the unpigmented, amœboid forms. It is frequently employed to designate both the pigmented and the unpigmented amœboid bodies, as well as the parasite in all of its forms. These amœboid bodies may be called, in general, hyaline forms or amœbæ.

As will be explained subsequently, it is only the quartan variety which is found in all its forms with equal frequency in the peripheral circulation and in the blood of internal organs; whereas segmenting tertian parasites are more abundant in the spleen and bone marrow than in the peripheral vessels, and the æstivo-autumnal parasite develops mainly in the internal organs, its segmenting forms being extremely rare in the peripheral circulation.

Each of the forms of the parasite which have been described as developing within the red blood corpuscles may also be found free in the plasma. They probably escape by rupture of the enveloping corpuscle, a process which one can often witness when examining the fresh blood microscopically. Extracorpuscular mature forms may possibly segment in the usual way, but there is no evidence that forms in the earlier stages may complete their cycle of development free in the plasma.

The important discovery was made by Golgi that all of one generation of the parasite form a group, the members of which develop

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[1] Plehn claims to have observed that the spores are actively motile and flagellated, but this statement is opposed to the observations of all others.

approximately at the same time, and that a definite relation exists between the phases of development of the parasite and the stages of malarial fever. The onset of a paroxysm corresponds to the ripening of one generation of the parasite. A few hours or shortly before the paroxysm segmenting forms appear, and enable the observer to predict the approaching paroxysm. The spores which are set free by the act of sporulation invade the red blood-corpuscles and start a fresh generation, which pursues during the paroxysm and the subsequent apyrexia so regular a development that in typical cases the experienced observer can tell approximately by examination of the blood the stage of the disease—that is, the time which has elapsed since the last paroxysm and the time when the next paroxysm may be expected.

It is not, however, always the case that the parasite develops with the regularity expressed by Golgi's law, and especially in the æstivo-autumnal fevers irregularities are very common. The simultaneous occurrence of two or more generations in different stages of development may render difficult the interpretation of the phases observed, although even here careful observation will enable the observer to draw correct conclusions in tertian and quartan fevers.

It has not been satisfactorily demonstrated that there occurs any other cycle of development of the malarial parasite in human beings than that which has been described, although the possibility of such an occurrence is by no means disproven. Canalis (1889) believes that he has found evidence that a second, slower cycle of development of the æstivo-autumnal parasite occurs, which is represented in certain of its phases by bodies of the crescentic group, to be described subsequently; and this view, with certain modifications, has been accepted by Golgi, Antolisei and Angelini, Grassi and Feletti, and Sacharoff. This doctrine is, however, opposed by many observers, and it does not at present rest upon sufficient evidence.

It seems necessary to suppose, on the basis of clinical evidence, that the malarial parasite may remain for months in a latent condition in the human body, and then begin to develop again, causing a relapse of the fever. As such relapses may occur in forms of malaria in which crescents do not appear, there must be in these cases some resistant organism other than bodies belonging to the group of crescents. We know nothing as to the nature of these resistant bodies. The hypothesis is advanced by Bignami that they may be spores which are enclosed within leucocytes and other cells, and which have become surrounded by a resistant membrane and have lost their usual staining properties.

Besides the forms which have already been described as representing phases of the regular sporulating cycle of development of the malarial parasite, there occur other forms which cannot at present be referred to any cycle of development. These other forms are—(1) crescentic bodies and fusiform, oval, and round bodies belonging to the same group; (2) flagellate bodies and free flagella; and (3) degenerative forms.

The crescentic and flagellate bodies, from their size and remarkable appearance, are the most striking forms of the parasite, and from the beginning have attracted much attention. Their significance, although there are many hypotheses concerning it, is not understood.

(1) The crescents develop only from the æstivo-autumnal parasites,

and will therefore be described in connection with these. They are never formed from quartan and tertian parasites.

(2) *Flagellate bodies*, on the other hand, may form from each variety of the parasite, tertian, quartan, or æstivo-autumnal. The weight of evidence is that they do not exist in the circulating blood, but develop after the blood has been withdrawn from the body, usually within ten to twenty minutes, sometimes earlier. Some observers have found them frequently, others only rarely. They are frequently found if the blood is examined at the right stage of the disease and time is allowed for their development. Councilman showed that they are more commonly found in blood aspirated by a hypodermic needle from the spleen than in the peripheral blood. They develop in tertian and quartan fevers from the mature, full-grown extracorpuscular forms—in tertian especially from swollen forms larger than the red blood-corpuscles. They are therefore found most frequently a short while before and during the paroxysm. In infections with the æstivo-autumnal parasite the flagellate bodies develop from round bodies belonging to the group of crescents, and do not occur in definite relation to the stage of the fever. Rarely intracorpuscular bodies may develop flagella.

The spherical bodies which become transformed into the flagellate bodies are always or nearly always pigmented. Marchiafava and Celli state that they once saw an unpigmented flagellate body. These bodies may be somewhat smaller or larger than the red blood-corpuscles, the size varying to some extent with the different varieties of the parasite, as will be explained later. The process of development of the flagella may be studied under the microscope. The pigment granules, which at first (æstivo-autumnal variety) may have been in repose, usually begin to dance about within the organism, often in a lively way. In the æstivo-autumnal variety they usually gather in the central part, but in the others they may be near the periphery or irregularly distributed. The spherical body may acquire an oscillatory or jerking movement. Projections may be formed and retracted at the periphery, and the whole edge may acquire a vigorous undulating movement. These changes are attributed to the movements of the flagella within the body or in its peripheral layers, and have been graphically compared by Richard to the struggles of an animal to get free. Suddenly the flagella shoot out from the periphery, and with their active lashing movements produce a violent commotion among the red blood-corpuscles and other small particles which may be in their neighborhood (Plate I. Figs. 22 and 41; Plate II. Figs. 43, 44).

The flagella are pale and thin, and present often at their extremities and along their course small olive-shaped swellings which may change their position. Here and there a pigment granule is occasionally seen in a flagellum. The flagella vary in size, number, and position. Their length may be three or four times the diameter of a red blood-corpuscle or not more than half that size. One to six may be attached to the spherical body. They may project from one side or from any part of the circumference of the body. Their movements may be somewhat rhythmical; they may become slow or even cease, and again start up.

Flagella may become detached and move about freely among the red blood-corpuscles. On account of their pallor such free flagella would usually be overlooked were it not for the commotion which they produce among the red blood-corpuscles. The motion of the flagella may be observed on the slide for half an hour, sometimes longer.

These flagellate bodies are the most startling forms of the malarial organism, and no one who sees them doubts for a moment that he is looking at a living parasite. It is not surprising that they attracted in an especial manner the attention of Laveran, who, as already mentioned, regarded the flagella as the most characteristic and perfect form of development of the parasite. Subsequent studies have not, however, tended to confirm the conception of Laveran as to their significance. As has already been made clear, the flagellated bodies do not belong to the regular sporulating cycle of development of the malarial parasite in the human blood. The most prominent theories as to their significance are the following:

(*a*) They are forms of degeneration or appearances belonging to the death-agony of the parasite. In support of this view it is urged that the flagellate bodies do not belong to any known cycle of development; that they are developed only outside of the human body; that they are developed from mature forms which are known frequently to undergo undoubted degeneration, such as hydropic swelling, vacuolation, and fragmentation, and which may already show beginning evidences of degeneration; that nuclear substance is absent from the flagella; and that similar appearances of extrusion of motile filaments in other unicellular organisms are known to zoölogists and are interpreted as degenerative.

(*b*) Sacharoff, from the study of their structure on stained specimens, believes that the flagella are extruded chromatin filaments derived from perverted karyokinetic nuclear division. He regards the process as degenerative.

(*c*) Dock suggests that the flagellate bodies "represent resting states of the organism, capable of existing independently, perhaps even of reproducing themselves, but also able, under favorable circumstances, of reproducing the typical growth of the parasite."

(*d*) Mannaberg's opinion is that the flagellate bodies may represent a state belonging to the saprophytic existence upon which the mature forms of the parasite enter soon after the blood is withdrawn from the body. On account of unsuitable conditions of environment they are unable to continue this existence in the blood outside of the body and soon perish. A similar view is advanced by Manson, who suggests that the flagellate bodies represent the first stage, and the detached flagella, in search of their appropriate host, represent the second stage of life of the parasite outside of the body. Manson[1] conjectures that the mosquito is the extracorporeal host of the malarial parasite, and he reports observations of Ross showing the development of flagellate forms in the stomach of mosquitos fed on malarial blood.

There are arguments for and against each of these theories. Reluctant as one may be to consider such striking forms as the flagellate bodies as phases of degeneration, the existing evidence seems upon the whole to be more in favor of this hypothesis than of any other which has been advanced. Still, if Sacharoff's observation as to the presence of nuclear material in the flagella be correct, the objection of Grassi and Feletti, that the flagella are incapable of reproductive development because the nucleus of the parasite does not divide and enter them, would be overthrown and the hypothesis of Mannaberg and Manson would become more probable. It is evident from the description of these bodies that the use of the word "flagella" to designate the motile filaments is of doubtful propriety, but it is the term commonly employed.

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[1] Manson: "The Goulstonian Lectures on the Life History of the Malaria Germ Outside the Human Body" (*The British Medical Journal*, 1896, March 14, 21, 28). Manson lays much emphasis upon supposed analogies between the malarial germ and the filaria sanguinis. Only future investigations can determine the correctness of Manson's hypothesis.

(3) There are various bodies, often seen in the examination of malarial blood, which are undoubtedly *degenerative forms* of the parasite, and others which are probably degenerative, although opinions concerning the latter are divided. The more common signs of degeneration of the parasite are vacuolation, pseudo-gemmation, fragmentation, deformities of shape, particularly swelling, granular condition of the protoplasm, certain alterations in the arrangement and appearance of the pigment, disappearance of nuclear material, defects and irregularities in staining, and changes in the refraction of the organism. These various degenerative changes produce forms too numerous to describe in detail. They have often been misinterpreted and described as special forms of the parasite, some of them, particularly certain vacuolated and budding forms, as special modes of reproduction.

Degenerations may occur in any form of the parasite, but they are particularly common in the extracorpuscular forms. Mannaberg describes the disintegration of young intracorpuscular forms, with disappearance of their nuclei. Fragmentation of forms extruded from the blood-corpuscles can sometimes be watched while examining fresh blood under the microscope (Plate I. Fig. 21). As a rule, only a certain number of the mature forms actually enter into reproductive segmentation, and many of the spores or segments perish. If all segmented and the offspring survived, the number of the parasites after a few paroxysms would become enormous. As a matter of fact, degenerations of full-grown parasites are often observed. An interesting form of such degeneration, found most frequently in the mature forms of the tertian variety, is the appearance of swollen, pigmented, so-called hydropic bodies, often much larger than red blood-corpuscles (Plate I. Figs. 18, 40), and sometimes containing vacuoles (Plate I. Figs. 18, 19, 23, 24, 40, and 42). Round bodies simulating spores are sometimes seen in these vacuoles, but on properly stained specimens they are devoid of the nuclear material of genuine spores. Pseudo-gemmation, or the appearance of sarcodic buds on the surface of the organisms, is doubtless a form of degeneration. Such buds may become separated, in the form of hyaline balls, from the parent organism (Plate I. Figs. 19, 20). These evidences of degeneration may appear also in crescents and bodies belonging to this group (Plate II. Figs. 40, 41) and in flagellate bodies. From the latter small hyaline balls with a flagellum attached may break off and move around actively. Such bodies might be mistaken for flagellated spores.

There is no good evidence that the malarial parasite ever multiplies by budding[1] or by simple cell-division. The only form of multiplication which has been demonstrated is that of sporulation, also called segmentation, already described, although it cannot be denied that other forms of reproduction may exist.

Various interesting degenerative changes are produced by the influence of quinine. These will be fully described under TREATMENT, *Action of Quinine on Malarial Parasites*, page 146.

As the malarial parasite passes its vegetative life mostly within the red blood-corpuscles, it is evident that it finds its food in this situation. This food may be appropriated both by intussusception and by diffusion. Evidence of intussusception is found in the occasional presence of fragments of the corpuscular substance within the body of the amœboid forms. Doubtless diffusion is the more important mode of nutrition of the parasite.

The question has been raised whether the parasite may develop in other cells of the body than the red blood-corpuscles. Nearly all forms of the parasite have been found enclosed in cells, chiefly leucocytes, splenic or medullary cells, and endothelial cells. As such included parasites often present evidences of degeneration, these appearances have been generally interpreted as referable to phagocytic destruction of the parasites, and such they unquestionably usually are. Golgi and Monti have, however, recently published observations intended to show that the æstivo-autumnal parasite may develop within endothelial and other cells, as will be explained in considering this variety of parasite.

The malarial parasite in the condition in which it exists in the human body is very susceptible to injurious agencies. It is quickly killed by the addition of distilled water and of dilute acids and alkalies. Under ordinary conditions it does not long survive in blood withdrawn from the body. Under certain special circumstances it has been kept apparently alive for two to four days, possibly for a week. Sacharoff observed amœboid movements in æstivo-autumnal hyaline bodies which had been for a week in the intestinal canal of leeches kept on ice, and he obtained a positive result by inoculating himself with malarial blood preserved in this way for four days in leeches. The tertian and quartan parasites were found to be less resistant than the æstivo-autumnal. Ripe bodies may segment in blood outside of the body, but no further development or multiplication of the parasites has been positively observed in the various attempts made to preserve or cultivate them. The parasite does not continue to develop and multiply in the human body after death.

Of course no inferences can be drawn from these observations as to the resistance of the parasite in its natural condition in the outer world. As to what this natural condition is we can only speculate. Grassi and Calandruccio have thought that certain species of amœbæ which they have observed in malarial districts might be the extraparasitic form. The failure of artificial cultivations and certain analogies drawn from the zoölogical characters of the parasite have led to the prevalent theory that the malarial parasite passes at least a part of its existence as a parasite in animal or vegetable organisms. Mention has already been made of Manson's hypothesis that the mosquito may be a host for the malarial parasite. That the germ is capable of entering upon some resistant phase of development seems highly probable in view of the evidence that malaria can be contracted from the air. There is no evidence that the malarial parasite is eliminated from the human body in a condition capable of infecting another individual or the locality. The disease, however, can be transmitted by inoculating into healthy individuals, either subcutaneously or intravenously, blood from a malarial patient.

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[1] Celli and Guarnieri for a time believed that spherical bodies of the crescentic phase may multiply by the formation of buds (gemmation), but they subsequently abandoned this view and adopted the now generally accepted opinion that these budding forms are degenerative. The "buds" are devoid of the structure of genuine spores.

UNITY OR PLURALITY OF THE MALARIAL PARASITE.

As has already been mentioned, there are two schools of doctrine as to the malarial parasite—the one led by Laveran holding that the malarial parasite is a single species with pleomorphic characters, the other believing that there are three or more species, or at least varieties, of malarial parasites. The observations upon which the latter doctrine is based originated with the Italians, and have been supported by investigations in this country and elsewhere.

Golgi in 1885 and 1886 first differentiated the parasite of quartan fever from that of tertian fever, and Marchiafava and Celli and Canalis in 1889 and 1890 differentiated the variety of parasite characteristic of æstivo-autumnal fever.[1] There is much difference of opinion as to the number of æstivo-autumnal parasites. All adherents of the doctrine of plurality agree that there are at least three varieties of malarial parasite —namely, the quartan, the tertian, and the æstivo-autumnal—distinguished from each other by morphological and biological characters to be subsequently described. The discovery by Golgi of the definite cycle of development of the malarial parasite and the recognition of several distinct varieties have done much to bring order out of the earlier chaotic condition when a multitude of parasitic bodies were described without knowledge of their significance or relations to each other. There remain, however, many unsolved problems which it may be expected that further investigations will clear up.

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[1] Marchiafava and Celli on the one hand, and Canalis on the other hand, have conducted a polemic as to which of them belongs the credit of first distinguishing the æstivo-autumnal parasite. The differentiation of this parasite was not made all at once, and with the same precision in all details, as in the case of Golgi's sharp separation of the quartan and tertian parasites. Golgi from the beginning of his researches (1885–86) suggested that the crescentic bodies belong to a special cycle of existence different from that of the tertian and quartan organisms, and noted their occurrence in irregular malarial fevers. Councilman in 1887 emphasized the association of crescents with remittent fevers and malarial cachexia. Golgi in February, 1889, definitely expressed the opinion that in addition to the malarial fevers caused by the quartan and the tertian parasites we must recognize another type of fever associated with unpigmented amœboid forms and crescents. On September 13, 1889, appeared a preliminary communication of Marchiafava and Celli, which must be regarded as furnishing the first clear and sharp description of the essential differential characters of the æstivo-autumnal parasite, with especial emphasis on the occurrence of unpigmented organisms. On October 10, 1889, appeared the preliminary communication of Canalis, in which likewise the essential characters of this parasite were described, and a greater emphasis was laid upon its relation to the crescents than had been done by Marchiafava and Celli. The full publication of Canalis anticipated by a short time the complete article of Marchiafava and Celli on the æstivo-autumnal parasite.

In opposition to the doctrine of plurality it is urged by Laveran that all of the so-called varieties of the parasite may be explained simply as phases of a single pleomorphic organism influenced by various conditions of environment, such as locality, season, individual predisposition, and various unknown circumstances. He contends that the characters upon which a division into separate varieties is based are insufficient for such a purpose and inconstant; that one so-called variety under certain conditions may be transformed into another; and that there is no definite, necessary relation between the types of fever, such as quartan, tertian, quotidian, irregular, continued, and the form of parasite present. The variations of the malarial parasite can be explained, he thinks, in large part by the varying rapidity of development. He emphasises the view that malaria with all its diverse manifestations is nevertheless clinically and anatomically one disease, and has always been so regarded. He argues that the experimental production of malaria by inoculation does not support the doctrine of plurality.

In considering the force of these objections it must be admitted that so long as we are unable to cultivate the malarial parasite artificially, and are ignorant of its life-history and the conditions of its existence outside of the human body, the possibility must be admitted that under certain conditions, at present unknown, one variety may be transformed into another. But, on the other hand, the existing evidence—and it is already considerable—goes to show that under the conditions which we can at present control and study each of the three principal varieties of the parasite preserves its identity and is not transformed into another variety; that is to say, there is no evidence that a quartan parasite ever becomes metamorphosed into a tertian, or either of these into an æstivo-autumnal parasite.

The principal arguments in support of this doctrine of plurality may be summarized as follows:

(1) Each well-established variety of parasite presents morphological and biological characters which suffice for its identification.

(2) Each variety of parasite corresponds to definite types of fever. Genuine quartan fever can be produced only by the quartan parasite. As will be explained in the clinical part of this article, other types of fever may be caused by more than one variety of parasite, and much complexity may result from multiple and mixed infections and various irregularities; but all of this does not prevent the recognition of certain fundamental types of fever especially characteristic of each variety of the parasite.

(3) Cases of pure infection with one variety of parasite have been carefully studied for weeks and months without any indication of the transformation of one variety into another (Calandruccio, Grassi and Feletti). Opportunities for such study are exceptional. The appearance of a second variety of parasite in localities where there is opportunity for renewed infection cannot of course be interpreted in favor of the metamorphosis of one variety into another.

(4) In certain localities only one or two of the varieties of the parasite are met with. In a few places only the quartan, or more frequently only the tertian, parasite is observed; in most places where malaria is mild and infrequent only tertian, and occasionally quartan, parasites,

with entire absence of æstivo-autumnal parasites, are found. Instances of this localized distribution of the parasites, which manifestly is a strong argument in favor of the doctrine of plurality, will be subsequently mentioned (page 99).

(5) Strong arguments in favor of the constancy of the varieties of the malarial parasite are furnished by the experimental production of malaria. Gerhardt in 1882 and 1883 (reported in 1884) was the first to produce malaria experimentally by the subcutaneous injection of blood obtained from malarial patients. At this time the malarial organism was not generally recognized. Since these first experiments similar ones have been repeated, usually in the manner of intravenous injections of malarial blood, with positive result in over thirty cases. The experiments before 1889 were made without determination of the exact variety of parasite injected and found in the experimental case. In 1889, Gualdi and Antolisei, without full knowledge of the critical nature of the experiment, injected two patients intravenously with 3 c.cm. of blood from a patient suffering with quartan fever and possessing quartan parasites. In each of the inoculated individuals irregular fever with æstivo-autumnal parasites developed. These two cases are constantly adduced as a main support of the doctrine of mutability of the varieties of the parasite, but unjustly so, for it was subsequently determined that the patient from whom the blood was obtained had previously suffered from irregular fever, and he subsequently developed characteristic æstivo-autumnal organisms, so that the experimenters themselves later expressed the opinion that at the time of the inoculation the patient furnishing the blood had combined quartan and æstivo-autumnal organisms, the latter being overlooked. In view of the uniform results yielded by the numerous subsequent experiments in support of the doctrine of immutability of the varieties of the parasite there can be little doubt that this later opinion of Gualdi and Antolisei is correct. It has been found regularly since these experiments that if blood containing only the tertian or the quartan or the æstivo-autumnal parasite be injected intravenously into a person unaffected with malaria, the variety of parasite injected, and only that variety, appears in the blood of the experimental case. When two varieties of parasite are injected, or when the malarial blood is injected into a patient already affected with a malarial organism other than that injected, then it usually happens that one variety supplants the other, most frequently the one injected supplanting that already existing in the inoculated individual. For such displacement of one organism by another we have numerous examples in bacterial infections.

The bearing of the inoculation experiments upon the determination of the periods of incubation of malaria will be considered in the clinical part of this article (pages 97, 98).

These already numerous inoculation experiments, showing the identity of the parasite in the experimental case with that in the blood used for injection, furnish the strongest existing arguments in favor of the plurality of the malarial parasites.[1]

Whether, accepting this doctrine, we shall designate the different types of the malarial organism as separate species or separate varieties is with our present knowledge a matter of secondary importance and of individual judgment. If it be admitted that under no existing circumstances one type is transformed into another, then we are justified in speaking of separate species of malarial parasites. As at present we can study only a small part of the conditions which surround the entire life-history of the parasite, it seems to the writer preferable to designate the different types as varieties rather than species.

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[1] Di Mattei: "Contributo allo Studio della Infezione Malarica Sperimentale nell' Uomo e negli Animali," *Arch. per le Scienze Mediche*, vol. xix. N. 4, 1895.

CLASSIFICATION.

We have already had occasion repeatedly to mention the division of the malarial parasites into three principal varieties—the quartan, the tertian, and the æstivo-autumnal. No further subdivision of the quartan variety has ever been suggested. Nor has any attempt been made to subdivide the tertian parasite originally described by Golgi; but, as it has since been found that the æstivo-autumnal parasite—or, according to some observers, one form of this parasite—may likewise produce tertian fever, the latter form of the æstivo-autumnal organism is designated by Marchiafava and Bignami as malignant tertian or æstivo-autumnal (summer-autumn) tertian, and the former is called mild or vernal (spring) or genuine tertian or Golgi's tertian parasite. This so-called æstivo-autumnal or malignant tertian is, however, in no sense a subdivision of the tertian parasite originally described by Golgi, which remains a well-differentiated, separate variety. When the name "tertian organism" is used without any epithet, it is always this variety which is meant.

The name "parasite of æstivo-autumnal fever," introduced by Marchiafava and Celli and already adopted by many writers, leaves much to be desired. It is intended to indicate that this form of the parasite is the cause of the malarial fevers prevailing in summer and autumn. This application, however, is correct only for certain localities, chiefly those warmer regions where severe as well as mild types of malaria occur. In localities where the prevailing type of the disease is mild at all seasons the summer and autumn malarial fevers are caused generally or exclusively by tertian or quartan parasites. Even in the warmer situations where the æstivo-autumnal parasite is common, not all of the summer-autumn fevers are caused by this parasite, but often a large proportion are caused by the ordinary tertian parasites. In subtropical and tropical regions the æstivo-autumnal parasites may occur in winter and spring fevers. It is evident that the epithet "æstivo-autumnal," as applied to a special variety of malarial parasite, is sufficiently designative for many localities, as, for example, the southern parts of the United States and Central and Southern Italy, but it is not so for all.

The term "parasite of æstivo-autumnal fever" does not at once suggest the relation of the parasite to a definite type of malarial fever, and is therefore out of harmony with the designations "parasite of quartan fever" and "parasite of tertian fever." But it is characteristic of a large proportion of the fevers caused by æstivo-autumnal organisms that they do not correspond to any definite type, but are notably irregular. Hence these organisms were designated by Golgi and by Sacharoff as the "parasite of irregular malarial fevers." But the objection to this latter name is that æstivo-autumnal organisms may cause typical quotidian and tertian fevers. Indeed, this is the only form of malarial parasite which, it is believed, may complete its cycle of development in twenty-four hours, and thus when present in only a single group or generation may cause quotidian fever.

As leading characters of the æstivo-autumnal organisms are their small size, their slight formation of pigment, and the ring-like shape of the amœboid forms, they are sometimes spoken of as the small malarial organisms (*forme piccole*), or the unpigmented, colorless, or slightly pigmented organisms, or the ring-like, annular organisms. They are also called the organisms of grave or pernicious malaria, although they may likewise cause mild types of the disease.

As it is to the group of æstivo-autumnal parasites that the crescents exclusively belong, these parasites have been described as the semilunar variety. They may be designated as crescent-producing. Hæmatozoön falciparum is suggested by the writer as a suitable technical name for this variety of parasite.[1]

The three varieties of the malarial parasite may therefore be technically designated—(1) *Hœmatozoön febris quartanœ;* (2) *Hœmatozoön febris tertianœ;* (3) *Hœmatozoön malariœ falciparum.* The name æstivo-autumnal parasite, as the more commonly used and generally understood designation, will, however, continue to be used, as well as the term "Hæmatozoön falciparum," in this article for the last-named variety.

There is no difference of opinion, except among the unicists, that the æstivo-autumnal organisms form a variety or group which is to be differentiated from both the quartan and the tertian organisms even more sharply than the tertian and the quartan are differentiated from each other. But the question as to the unity or the plurality of the æstivo-autumnal organisms is still an open one, and is the most important unsolved problem relating to the divisions of malarial parasites. Its solution is attended with unusual difficulties, but we may reasonably expect that they will be surmounted by future investigations.

In distinction from the quartan and the tertian organisms the æstivo-autumnal are often irregular and atypical in their cycle of development. Some, it is believed, may complete their cycle in twenty-four hours, others in forty-eight or a longer period: their tendency to develop simultaneously in well-defined generations is far less marked than is the case with tertian and quartan organisms, so that several or all phases of development of æstivo-autumnal forms may be observed in the internal organs at the same time. The occurrence of multiple groups of the parasite is common. Forms appear which pass through their amœboid, mature, and segmenting phases without any formation of pigment within the parasite. The development takes place largely in the internal organs. The development of crescents occurs at a variable period after the onset of the disease, but rarely in less than a week. Corresponding to these variations and irregularities the types of fever with which æstivo-autumnal organisms are associated are various and irregular.

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[1] The name Hæmatozoön falciforme suggested by Antolisei and Angelini is objectionable, as it implies that the shape is always falciform, and is applicable only to the crescentic forms. The adjective "falciparum" (*falx*, "sickle," *parire*, "to bring forth," "to produce"), on the other hand, indicates that the property of forming crescents is a distinctive character of the organism, and it is therefore applicable to the variety of the parasite which possesses exclusively this property.

The attempt has been made to deduce certain laws controlling these variations and apparent irregularities, and to subdivide the æstivo-autumnal organisms into certain varieties or subvarieties, but there is little agreement of opinion as to this subdivision.

The following are the principal divisions of the malarial parasite which have been proposed, the essential differences in these various divisions relating, of course, to the different views held concerning the æstivo-autumnal organisms:

I. Marchiafava and Celli (1889) recognized a short cycle of development of the æstivo-autumnal parasite, unaccompanied by development of pigment, and a longer cycle with formation of a few pigment granules. Marchiafava and Bignami (1891) make two varieties of this parasite—viz. the amœba of æstivo-autumnal quotidian, with a twenty-four-hour cycle, and the amœba of æstivo-autumnal tertian, with a forty-eight-hour cycle—*Amœba febris quotidianæ* and *Amœba febris tertianæ æstivo-autumnalis*. The latter variety is the malignant tertian organism of these authors. The main differences between these varieties, according to Marchiafava and Bignami, relate to the length of the cycle of development, but there are claimed to be also minor morphological and biological differences to be mentioned subsequently (page 51).

These authors, therefore, make four different varieties of the malarial parasite. They divide the malarial fevers into two main groups:

1. Mild malarial fevers which prevail in winter and spring. These are—

(*a*) Quartan fever (with its varieties of double and triple quartan). This is caused by the *Amœba febris quartanæ* (Golgi), which completes its life cycle in seventy-two hours.

(*b*) Tertian fever (with double tertian and rarely certain subcontinued fevers). This is caused by the *Amœba febris tertianæ* (Golgi), which completes its life cycle in forty-eight hours.

2. Severe or æstivo-autumnal fevers, including the pernicious and most of the subcontinued fevers. This group comprises—

(*a*) Æstivo-autumnal quotidian fever (to be distinguished from quotidians of tertian and of quartan origin), caused by the *Amœba febris quotidianæ*, which completes its cycle in twenty-four hours. This is the only variety of malarial parasite which can complete its life cycle in so short a period as twenty-four hours.

(*b*) Æstivo-autumnal or malignant tertian fever, caused by the *Amœba febris tertianæ æstivo-autumnalis*, which completes its cycle in forty-eight hours. Most of the pernicious cases belong to this variety, the remainder to the æstivo-autumnal quotidian variety.

II. Canalis (1889) does not subdivide into varieties the æstivo-autumnal parasite, which he calls the "semilunar variety," but he considers that it has two cycles of development: (*a*) a rapid cycle with the usual phases of amœboid, mature, segmenting forms and spores, and (*b*) a slower cycle associated with the development of crescentic bodies, which he considers to be reproductive and to represent one phase in this second cycle. A similar view is held by Antolisei and Angelini.

III. Grassi and Feletti (1890) regard the crescent-producing forms as an entirely separate species, which they call *Laverania malariæ*, and which they distinguish both from the directly spore-forming unpigmented æstivo-autumnal forms, which they call *Hæmamœba immaculata*, and from similar rapidly developing, but pigmented, æstivo-autumnal parasites, without crescents, which they call *Hæmamœba præcox*. Their classification of the malarial parasite is as follows: (*a*) *Hæmamœba malariæ*, identical with the quartan parasite; (*b*) *Hæmamœba vivax*, which is identical with the tertian parasite of Golgi; (*c*) *Hæmamœba præcox*, a form of the æstivo-autumnal parasite, giving rise to quotidian fever; (*d*) *Hæmamœba immaculata*, similar to the preceding, but without development of pigment; (*e*) *Laverania malariæ*, the crescent-producing variety, giving rise to irregular fevers.

Sacharoff formerly regarded the crescents as belonging to a separate species of malarial parasite, and adopted the following classification: (*a*) *Hæmamœba febris quartanæ* (Golgi), (*b*) *Hæmamœba febris tertianæ* (Golgi), (*c*) *Hæmamœba præcox* (Grassi), (*d*) *Laverania* (Grassi). Recently (1896) he holds that all variations of the æstivo-autumnal parasite are modifications of a single variety due, mainly, to the development of the parasite within nucleated red blood-corpuscles.

IV. Mannaberg (1893) accepts Marchiafava and Bignami's division of æstivo-autumnal parasites into quotidian and tertian, and also adopts Grassi and Feletti's division into pigmented and unpigmented quotidian parasites. He does not, however, consider the crescents as belonging to a species or variety distinct from these, but considers them as developing from each of these three divisions of æstivo-autumnal parasites. He has a peculiar view as to the origin of the crescents from conjugation of cells, and regards them, therefore, as forms of syzygia. He divides the malarial parasites into two groups—the *first group*, with sporulation and without syzygia, comprising (*a*) the quartan and (*b*) the tertian parasites of Golgi; the *second group*, with sporulation and with syzygia, comprising (*a*) the pigmented quotidian parasite, (*b*) the unpigmented quotidian parasite, and (*c*) the malignant tertian parasite.

V. Golgi (1893), an admirable and successful investigator of the malarial parasites, does not consider the semilunar forms as belonging to a species or variety distinct from the ordinary sporulating æstivo-autumnal parasite. He attempts no subdivision of the æstivo-autumnal parasite. His conception of the mode of development of this parasite differs in essential points from that of Marchiafava and Bignami and of most other investigators, as will be explained in considering the special characters of the æstivo-autumnal parasite.

The following statement of Golgi's classification of the malarial fevers is quoted from Thayer and Hewetson's work on *The Malarial Fevers of Baltimore*, already cited.[1] Golgi divides the malarial fevers into two groups:

(1) Fevers the pathogenesis of which is connected with parasites which have their principal habitat in the circulating blood, where, by preference, they accomplish the phases of their cycle of existence.

(2) Fevers the pathogenesis of which is connected with parasites

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[1] The writer wishes to acknowledge his indebtedness to this excellent monograph for much valuable assistance in the preparation of this article.

which have their chief seats in the internal organs, particularly the bone marrow and the spleen, where, by preference, they accomplish their cycle of existence in conditions of relative stability.

(1) The fevers of the first group are unquestionably associated with different species or varieties of the parasite—viz. (*a*) the quartan parasite; (*b*) the tertian parasite.

(2) "To the second group belong the fevers which appear clinically under multiform types, very often irregular, of which for the present it is impossible to make a grouping based upon an ascertained biology or cycle of development of the parasite. . . . We are dealing in these cases with generations of parasites which, occurring in the parenchyma of organs in different stages of development, give origin, at periods of a certain regularity or in a more or less continuous succession, to colonies of young forms which, in large or small numbers or in insignificant quantity, may escape into the blood current, permitting one to discover by microscopical examination of the blood the presence of the small endoglobular amœbæ." Golgi refers to the crescents as "forms the biology of which has not yet been well determined."

VI. Thayer and Hewetson (1895) were likewise unable to confirm Marchiafava and Bignami's subdivision of the æstivo-autumnal parasite into a quotidian and a tertian variety. They say: "We have been unable to trace a constant length of the cycle of development, and we have been unable further to separate two or more types of the [æstivo-autumnal] parasite depending either upon the length of the cycle of development or upon any other morphological or biological differences. We believe that the length of the cycle varies greatly in different cases, lasting usually from twenty-four hours, or even a little less, to forty-eight hours or more. After the infection is five days or a week old certain of the organisms, instead of segmenting, pursue a further growth, developing into the hyaline, refractive, ovoid, and crescentic bodies." They do not feel justified in making any positive statement as to the significance or capacity of reproductive development of the crescentic bodies.

The question has been raised whether in tropical regions, where pernicious types of malaria are common, any form of malarial parasite different from those already mentioned occurs. The observations of Van Dyke Carter, Dock, van der Scheer, Plehn, and others show that the same parasites are found in India, Panama, Java, and other tropical countries as elsewhere. The negative reports which have been published are referable doubtless to insufficient training in such examinations on the part of the observers. The fact that a large part of the tropical malarial fevers are caused by æstivo-autumnal organisms which appear in the red blood-corpuscles as small, pale, feebly-staining, delicate, diaphanous, often unpigmented amœboid rings of hyaline protoplasm, difficult to detect in many cases, and sometimes scanty or at times even absent, will account for many of these negative observations.

The singular distribution of the hæmoglobinuric type of pernicious malarial fevers in certain definite localities suggests the possibility that this may be caused by a special type of organism. The sporadic cases of malarial hæmoglobinuria examined in Italy have shown, however, ordinary æstivo-autumnal organisms. Plehn[1] found in cases of black-water fever occurring on the West Coast of Africa small, annular amœboid forms, staining with great difficulty and never pigmented, in the red blood-corpuscles. "Out of the amœba there develops by thickening of the peripheral zone an oval or egg-shaped body, with well-staining double contour. In course of time this divides into five or six small oval forms, staining at one pole, which, when they are set free, move about with great rapidity in the blood. These probably develop into the amœboid forms." The organism never attained a size larger than one quarter of the red blood-corpuscle. Crescents were occasionally found. Plehn seems to regard this organism as allied to, but not identical with, the æstivo-autumnal parasite described by Italian writers. Although his description presents certain peculiarities of the parasite which he observed in the pernicious malarial hæmoglobinuria and other pernicious fevers of the West Coast of Africa, especially the constant absence of pigment, the extremely small size, the sporulation in the blood, and the apparently motile spores,[2] nevertheless it is not sufficiently complete and satisfactory to justify the inference that the organism differs from forms of the ordinary æstivo-autumnal parasite as previously observed.

From the preceding review of the various investigations and opinions concerning the divisions or varieties of the malarial parasite, especially of the æstivo-autumnal form, we may draw the conclusion that whereas the separation into quartan, tertian, and æstivo-autumnal varieties rests upon a sound basis of fact, the various attempts to further subdivide the æstivo- autumnal group have not as yet been sufficiently successful to justify our acceptance at the present time of any of these subdivisions. There is, however, some reason to believe that this last group, as at present constituted, may comprise varieties which will hereafter be satisfactorily differentiated from each other.

We will now consider the special characters of each of the three varieties of the malarial parasite.

I. THE PARASITE OF QUARTAN FEVER (HÆMATOZOÖN FEBRIS QUARTANÆ) (PLATE I. FIGS. 25–42).

In most malarial regions this is the rarest form of the malarial parasite, but there are certain places (none of these have been recognized in this country) where it is the prevailing variety. Being particularly common in the neighborhood of Pavia in Italy, the quartan parasite was the first to be differentiated and described by Golgi (1885–86), to whose masterly description nothing of essential importance has been added by subsequent investigators, with the exception of certain details of intimate structure.

The quartan parasite completes its cycle of development in seventy-two hours and entirely within the circulating blood. The youngest forms of the parasite are small, amœboid, when at rest discoidal, hyaline bodies, within the red blood-corpuscles. They are about one-fifth to one-fourth the size of the red blood-corpuscle (Plate I. Fig. 26). The central part of the body may appear paler than the peripheral. These unpigmented, youngest forms are found during and for several hours after the paroxysm; they may begin to appear two hours before the paroxysm. The very earliest forms are not to be distinguished from the youngest tertian parasites, but as they begin to develop they present a sharper outline and somewhat more refractive appearance, and their amœboid movements are more sluggish and restricted than those of the corresponding stages of the tertian organism. These movements become more active on the warm stage of the microscope. The presence of more than one parasite in a red blood-corpuscle is sometimes observed.

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[1] Plehn: "Ueber das Schwarzwasserfieber an der afrikanischen Westküste," *Deutsche med. Wochenschrift*, 1895, Nos. 25, 26, 27.

[2] It may here be mentioned that Plehn considers that the spores of all varieties of the malarial parasite are flagellated—a view which has not been confirmed by other observers.

Shortly, or within twelve to eighteen hours, after the paroxysm pigment granules appear within these hyaline bodies, which continue to increase slowly in size, and for a while to exhibit lazy amœboid movements (Plate I. Figs. 27, 28, 29). The pigment appears in the form of brownish or black rods and grains, which are coarser and darker than those seen in tertian parasites. The rod form of pigment is less common than in the tertian organism. These pigment granules are arranged generally in the peripheral part of the parasite, and they present only a sluggish movement in comparison with the active motion of the pigment in the tertian parasite. With the gradual increase in size of the hyaline bodies and in the amount of contained pigment the red blood-corpuscles enclosing them may appear unchanged, or often they become a little smaller, more refractive, and deeper in color, which may be somewhat greenish or coppery in tint (Plate I. Figs. 28, 29). There is not that tendency to decolorization and swelling of the infected red blood-corpuscles which is noticed in the case of the tertian parasite, although in the more advanced stages of development there is usually some loss of color in red corpuscles containing quartan organisms.

In the process of development the amœboid movements cease, and the parasite appears as a quiescent, pigmented, spherical, or ovoid body occupying perhaps one-half to two-thirds of the red corpuscle (Plate I. Figs. 30, 31). Such bodies are usually seen within forty-eight hours after the paroxysm. These bodies continue to grow, and when they have reached their full development in sixty to seventy hours after the paroxysm they are somewhat smaller than the normal red blood-corpuscles. These full-grown forms are spherical or ovoid, refractive, hyaline bodies, with nearly or quite motionless dark pigment granules of variable size, but coarser than in the tertian parasite, and with a tendency to peripheral arrangement, but at times irregularly distributed. Around these bodies a thin layer of the colored, refractive substance of the red blood-corpuscle can usually still be seen (Plate I. Figs. 32, 33, 34), or the hæmoglobin may be entirely removed, so that only a delicate, thin, colorless rim or line surrounding the parasite is all that is left of the original red blood-corpuscle. In unstained specimens these latter forms often appear to be free in the plasma (Plate I. Fig. 35), and are sometimes spoken of as free bodies, which may also occur.

In six or eight to ten hours before the febrile paroxysm the first phases of reproduction begin to appear. These are ushered in by the gradual withdrawal of the pigment from the periphery toward the centre of the body. The pigment in this process is often arranged in definite radial striæ (Plate I. Fig. 36). Such regular stellate arrangements of the pigment as are seen in this stage of the quartan parasite are rarely, if ever, observed in the tertian (Thayer and Hewetson). Finally the pigment is concentrated into a central mass of granules or a solid block of coalesced pigment, less frequently into two or more collections, and the organisms assume a somewhat more refractive and slightly granular appearance.

At the same time or soon afterward radial divisional striæ begin to appear in the periphery (Plate I. Fig. 37), and quickly extend to the central part of the parasite, whereby the substance of the spherical organism becomes divided into six to twelve ovoid or pear-shaped segments arranged with characteristic and exquisite regularity around the central mass of pigment like the petals of a daisy (rosettes of Golgi) (Plate I. Fig. 38). In each of the segments can be seen a small round glistening body which represents the nucleus or nuclear material. The pyriform segments assume rapidly a round or oval shape, and become separated from the central mass and from each other. The delicate enveloping membrane, which may not be recognized on unstained specimens, derived from the red blood-corpuscle ruptures, or it may previously have disappeared, and the small round or oval bodies, each provided with a bright nucleiform dot, are set free in the plasma (Plate I. Fig. 39). These bodies are the so-called spores. Simultaneously with this process of sporulation young amœboid hyaline bodies, formed directly from the spores, make their appearance in the red blood-corpuscles, and the cycle of development is completed and another cycle is begun.

Segmenting or sporulating forms of the parasite may appear six or eight hours before the paroxysm, and are most abundant shortly before and during the onset of the paroxysm. It is of course not to be understood that all of the parasites of one group pass through their developmental phases and mature at exactly the same moment. One parasite of the group may be several hours in advance of another, but this does not interfere with the recognition of distinct groups or generations, each standing in definite relation to a paroxysm, or with the establishment of Golgi's law that the onset of each paroxysm corresponds to the maturation of one group of organisms.

The cycle of development of the quartan parasite is attended with fewer irregularities than that of any other variety of the malarial parasite. Nevertheless, certain irregularities may occur. As pointed out by Antolisei, segmentation may occur exceptionally in pigmented bodies considerably smaller than the usual full-grown forms, containing less pigment and filling only a part of the red blood-corpuscle. Here the segments do not usually exceed four to six or eight. The accumulation of pigment in the segmenting forms may be peripheral, or distributed between the spores, or otherwise irregular.

As the quartan parasite completes its development entirely within the circulating blood, there is no appreciable difference at any stage between the splenic and the peripheral blood as regards the number and variety of the parasitic forms observed. Moreover, segmenting forms of the quartan parasite are often seen in small number in the blood at a period before the total number of organisms is sufficiently large to produce by their ripening a paroxysm, whereas segmenting tertian parasites are very rarely seen in the peripheral blood without the occurrence of a paroxysm in relation to the segmenting forms.

Not all of the mature forms proceed to sporulation. Some, especially those which may have escaped from the red corpuscles, swell up, become transparent and larger than a red blood-corpuscle, and present irregularly distributed and actively moving pigment granules (Plate I. Fig. 40). These swollen, hydropic forms are probably sterile. It can often be seen in examining these bodies in fresh blood that the pigment becomes quiescent, the outlines of the body become irregular and indistinct, and evidently cadaveric forms result. Or these bodies may break up into a number of fragments which become misshapen and indistinct, or the whole body may become vacuolated, as is represented in Plate I. Fig. 42. Bodies more or less resembling spores, but without the nuclear structure of spores, may appear in these vacuoles.

As may occur with any variety of the malarial parasite, the mature forms of the quartan parasite, instead of sporulating, may develop into flagellate bodies in the manner already described. These bodies are smaller and contain coarser pigment than the flagellate forms of the tertian parasite. (Compare Plate I. Fig. 41 and Plate I. Fig. 22.) Degenerated and flagellate forms are less common in quartan than in tertian infections.

Not only may mature forms degenerate in the ways described, but forms in earlier stages of development may be liberated from the red corpuscles and likewise degenerate.

The phenomena of phagocytosis are observed with regularity during and for some hours after the paroxysm in quartan as well as in other malarial infections. The pigment set free by the process of sporulation is taken up by phagocytes. Extracorpuscular organisms, particularly the various degenerated forms, are engulfed by phagocytes. The assault on the flagellate bodies by leucocytes can be watched with interest on the slide of fresh blood. The leucocytes can also be seen to take up segmenting bodies and spores when the specimen of blood is kept for a while. The details and the significance of these phagocytic phenomena will be considered subsequently (page 65).

The intimate structure of the quartan and other malarial parasites, as revealed by methods of staining, will also be described subsequently.

Two or more groups of quartan parasites are often present in the blood at the same time, causing double and triple quartan infections. On account of the regularity in the development of the quartan parasite, anticipating, retarding, and irregular fevers are less common in quartan than in the other malarial infections. Careful examination of the blood enables the observer to recognize the presence of two or more groups of the parasite by noting the simultaneous occurrence of bodies in noticeably different stages of development; as, for example, during the paroxysm the association of segmenting and young hyaline bodies with half-grown pigmented bodies.

II. THE PARASITE OF TERTIAN FEVER (HÆMATOZOÖN FEBRIS TERTIANÆ) (PLATE I. FIGS. 1–24).

This variety of the malarial parasite is common in most malarial regions. Where only mild types of malaria occur it is, as a rule, the prevailing, and sometimes the sole, variety observed. The tertian and the quartan parasites cause most, or in some places all, of the winter and spring intermittents, but they, and especially the tertian parasite, may cause in districts of even severe malaria not a few of the malarial fevers of summer and autumn, although the more severe and irregular of these latter fevers are caused chiefly by the æstivo-autumnal parasite. The tertian parasite may, however, produce severe, as well as mild, types of malaria.

The tertian parasite was differentiated from the quartan and described in its essential characters by Golgi in 1886 and 1889. Other observers, particularly Antolisei (1889–90) and Bastianelli and Bignami (1890), have added to, and in some points corrected, Golgi's first description.

The chief points to be emphasized in this description of the tertian parasite are those which distinguish it from the quartan parasite. Unlike the quartan parasite, certain stages of development of the tertian—namely, those concerned with sporulation—take place by preference in the spleen and the bone marrow, although segmenting forms are seen also in the peripheral blood. The cycle of development is completed in forty-eight hours.

During the paroxysm or shortly after it small, unpigmented, hyaline, amœboid bodies are found within the red blood-corpuscles, of which they are about one-fifth to one-fourth the size (Plate I. Figs. 2 and 3). Usually one hyaline body is found, but not very infrequently two or more are present, in a single blood-corpuscle. The tertian amœbæ, especially in their pigmented stage, change their shape and position within the corpuscles much more actively than the quartan amœbæ, these movements being vigorous at ordinary room temperature. Several branching pseudopodia are sent out, often reaching nearly or quite the periphery of the corpuscle, and are retracted. All sorts of shapes may thus be assumed by the parasite, which with its long branching processes may seem to pervade nearly the whole corpuscle. By the union of two pseudopodia the shape may be that of a ring enclosing a bit of the corpuscular substance (Plate I. Fig. 5). The tertian amœbæ are paler, less sharply outlined, than the quartan (compare the two varieties in Plate I.). In a short time fine reddish-brown or yellowish-brown rods and granules of pigment, varying somewhat in size, appear in the margins of the amœbæ (Plate I. Fig. 5). Pigment granules often collect in the bulbous ends of pseudopodia (Plate I. Figs. 6 and 7), and the intervening parts of the pseudopodia may be so thin and delicate as to be readily overlooked, so that the appearance may be that of several distinct bodies within one red blood-corpuscle. Careful examination will, however, detect the fine connecting processes or the retraction of the apparently separate bodies into the substance of one parasite. Two or more parasites may, however, be present occasionally within one red corpuscle (Plate I. Fig. 4). The pigment is in finer grains and rods, and of a lighter, somewhat different, tint in the tertian, than in the quartan parasite. (See Plate I.) It is also in much more active movement in the tertian amœbæ. This movement is not altogether like the Brunonian or molecular motion, and is probably due to intrinsic protoplasmic movements or currents.

With the continued growth and increased pigmentation of the amœbæ the infected corpuscles as a rule become distinctly swollen and paler than normal—a change which may be already indicated even with quite small pigmented forms, and which is one of the most distinctive characters of the tertian parasite (Plate I. Figs. 4–9). Occasionally the enveloping corpuscle is not noticeably swollen or altered, and exceptionally it may even shrink and acquire something of the brassy appearance commonly seen with red corpuscles infected with the æstivo-autumnal parasite.

On the day of apyrexia the parasite, now with somewhat sharper contour and more richly pigmented, may attain a size equalling one-half to two-thirds that of the infected blood-corpuscle. The amœboid movements have become more sluggish, but they persist in stages of development corresponding to which forms of the quartan parasite have become quiescent. The pigment continues in active motion.

The fully developed parasite is about the size of a normal red corpuscle, sometimes a little smaller, sometimes somewhat larger, and it is therefore smaller than the swollen corpuscle in which it is contained. It is nearly or quite spherical in shape, and without amœbic movements. The pigment for a while preserves its marginal arrangement or less frequently is irregularly distributed (Plate I. Fig. 9). The expanded red blood-corpuscle enveloping the parasite becomes still paler.

These fully grown forms change into the presegmenting bodies by the collection of the pigment, which has already become quiescent, into a mass of granules or into a solid block situated usually in or near the centre or sometimes near or at the margin. As with the other varieties of the malarial parasite, the pigment with the development of the parasite becomes coarser, and the delicate rod-like forms of pigment become relatively less numerous. These spherical bodies with central pigment clumps are more refractive than is the parasite in preceding stages of development. Stained specimens show that in these presegmenting bodies there appear multiple, deeply staining chromatin granules, which represent nuclear substance, and which are the first indication of the inception of sporulation.

This phase of segmentation presents more variation than is observed in the quartan parasite. Sometimes it begins with the appearance of radial striation extending from the periphery to the centre, and proceeds by a division of the substance of the parasite into twelve to twenty or even more segments arranged in a rosette form around the central clump of pigment. A little later the pigment clump is surrounded by a group of small round bodies, which are the spores. More commonly, without the formation of such regular figures, the protoplasm breaks up into a mass of fourteen to twenty or more spores. Sometimes one sees an outer and an inner ring of spores concentrically arranged around the central mass of pigment. The larger number of segments or spores formed by the tertian as contrasted with the quartan parasite is an important differential characteristic.

The modes of segmentation described (Plate I. Figs. 10–14) correspond in the main to Golgi's second type of segmentation. His first mode of segmentation of the tertian parasite has not been noted by other observers. It is as follows: After the collection of the pigment in the centre the organism is differentiated into a peripheral zone sharply separated from a central body containing the pigment. The peripheral ring becomes radially striated, and then divides into fifteen to twenty small hyaline segments. The central pigmented body does not segment, but remains behind after the separation of the spores. Golgi's third variety of segmentation is now generally recognized as a process of degenerative vacuolation.

Sometimes the segmenting bodies show, instead of one central accumulation of pigment, two or more clumps excentrically placed, or the pigment may be concentrated in the periphery or distributed between the spores or otherwise irregularly arranged.

The spores are set free by rupture of the enveloping membrane derived from the red corpuscle, or this membrane may have disappeared before the segmentation is completed. The individual spores are somewhat smaller than those of the quartan parasite. They usually show a refractive nucleiform dot, which is, as a rule, less distinct than in the quartan spores.

Coincidently with sporulation the young, colorless amœbæ, formed from the spores, make their appearance in the red blood-corpuscles and start on a fresh cycle of development.

The segmenting bodies may make their appearance several hours before the paroxysm. They are most numerous shortly before and during the onset of the paroxysm. They may be scanty in the peripheral blood, for the process of sporulation takes place largely in the internal organs. The red corpuscles containing mature and presegmenting bodies accumulate especially in the spleen and the bone marrow, and there the organisms complete their reproductive development. During most of the period of apyrexia no noticeable difference is observed in the number and kinds of parasites between the peripheral blood and that withdrawn by hypodermic syringe from the spleen. But shortly before and during the paroxysm far more ripe and sporulating forms are found in the splenic than in the peripheral blood.

Precocious segmentation into five to ten spores may occur in bodies, sometimes containing only a grain or two of pigment, which have not attained a size exceeding one-half to two-thirds that of the red blood-corpuscles (Plate I. Figs. 16, 17), the usual size of a segmenting body being about that of a red corpuscle, but sometimes considerably larger. Such immature forms of segmentation are associated by Bastianelli and Bignami with anticipating fevers, but Mannaberg and Thayer and Hewetson, although not inclined to discredit this interpretation, were unable to convince themselves of this relation.

Partly developed and mature tertian parasites are often seen free in the plasma. Swollen, transparent, extracorpuscular forms, which may attain the size of large leucocytes, and which contain scattered dancing pigment granules, are generally considered to be degenerative or incapable of reproductive development (Plate I. Fig. 18). These so-called hydropic forms are considerably larger and paler and more common than the similar forms of the quartan parasite. These swollen, richly pigmented forms are very common in tertian infections. In general, the various forms of degeneration which have already been described, such as fragmentation, vacuolation, pseudo-gemmation (Plate I. Figs. 19, 20, 21, 23, 24), are more common with the tertian than the quartan parasite. Flagellate bodies are likewise more common. They are, as a rule, larger and contain finer pigment than the quartan flagellates (Plate I. Fig. 22). They develop chiefly from the round, swollen, extracorpuscular forms with scattered pigment, although flagella have been observed to develop from forms still surrounded with a distinct layer of hæmoglobin-containing substance of the red blood-corpuscle. Flagellate bodies are most abundant in blood withdrawn from the spleen shortly before and during the paroxysm. Phagocytosis occurs with the same regularity and with similar phenomena in tertian as in quartan infections.

Infection with two groups of tertian parasites (double tertian), as described for quartan infection, is more common than with a single group, especially in the later period of the malarial season in the spring and in summer and autumn. The resulting type of fever is quotidian. In some cases there seem to be several irregularly distributed generations causing remittent or subcontinued fevers. It is not necessary to attribute the presence of two or more groups of the same variety of parasite to corresponding multiple infections from without. There is evidence that certain members of a group may, in their development, lag behind or advance beyond others of the same group, and in course of time by further multiplication may constitute a separate group capable of causing its own paroxysms of fever. It is remarkable, however, that the second group should be separated in its cycle of development by such definite intervals from the first as we usually observe in quotidian fevers of tertian origin. Genuine mixed infections with malarial parasites, the most frequent combination being that of the tertian and of the æstivo-autumnal parasites, are not very uncommon.

The length of the cycle of development of the tertian parasite may occasionally be noticeably shorter than forty-eight hours, perhaps only forty hours or less, or, on the other hand, it may be longer than the normal period. This may explain the anticipating and the postponing fevers.

III. THE PARASITE OF ÆSTIVO-AUTUMNAL FEVER (HÆMATOZOÖN FALCIPARUM) (PLATE II.).

This was first clearly differentiated from other varieties of the malarial parasite by Marchiafava and Celli (1889), and was subsequently more fully described by the same authors and by Canalis (1889–90). (See footnote, page 32.) The extensive literature concerning the parasitology of malaria during the last six years has been concerned to a large extent with this variety, but we are still far from possessing so full and accurate knowledge regarding the characters and development of the Hæmatozoön falciparum as regarding those of the quartan and tertian parasites. Such knowledge is much to be desired in view of the frequency of the æstivo-autumnal parasite in regions, such as the southern part of the United States, where the more severe types of malaria occur, and of the almost exclusive association of this parasite with pernicious malarial fevers.

Chief reasons for the difficulty in investigating the entire life history of the Hæmatozoön falciparum are that it develops mainly within the internal organs and often in multiple groups, and that the later reproductive phases of development are met with in the circulating blood only very exceptionally. Under the *Classification* of the malarial parasites we have already presented the more important opinions which have been advanced concerning possible subdivisions of the æstivo-autumnal variety (page 35 *et seq.*).

The youngest forms of this parasite are small hyaline bodies, about one-sixth the diameter of a red blood-corpuscle, which make their appearance in the blood-corpuscles during or shortly after the paroxysm. It is not uncommon to find two or more hyaline bodies in a single corpuscle. These æstivo-autumnal hyaline bodies are in general the smallest forms of the malarial parasite which are observed in the red blood-corpuscle (Plate II. Figs. 1 and 2). The youngest forms may be quiescent, but as they develop they manifest amœboid movements resembling in their activity those of the tertian amœbæ.

The young æstivo-autumnal amœbæ may not be readily distinguishable from the similar forms of the quartan and tertian parasites. Particularly characteristic, however, of the young hyaline forms of the Hæmatozoön falciparum when in repose and in stained specimens is the ring shape. The appearance in fresh specimens is that of a somewhat refractive, clear, hyaline ring, usually thicker on one side, surrounding a small round central, or oftener excentric, shaded part, or sometimes two or three such parts, through which the color of the red corpuscle shows. In stained specimens the ring appears thinner than in fresh specimens, and the central or excentric part is unstained, while a minute deeply stained granule is situated in the outer ring.

The study of the further development of these forms, especially on stained specimens, has demonstrated that these apparently annular bodies are not actual rings, as some have supposed, enclosing a bit of the red corpuscle, but that the clear area which does not stain is a transparent part of the organism, which, as will be subsequently explained, some regard as the nucleus. Actual rings, however, as has already been mentioned, may be formed by the junction of pseudopodia, which thereby enclose some of the corpuscular substance, but such is not the explanation of the typical annular appearance of the æstivo-autumnal hyaline bodies. It is not uncommon to find free hyaline bodies in the blood plasma.

These hyaline bodies may, while under observation, become somewhat expanded and paler and lose their annular appearance, and again resume the ring shape. While the very smallest intracorpuscular hyaline bodies may present no amœboid movements, as they grow larger these movements become active. Hyaline bodies are occasionally observed to change their position within the corpuscle without change in their shape. Manifold shapes are assumed during the amœboid movements (Plate II. Figs. 4–6).

Usually in the course of development a few very fine dark reddish-brown or black pigment granules appear in the outer layer of the hyaline bodies (Plate II. Figs. 8–12). They may be situated near the periphery or on the inner margin of the ring near the clear part. Sometimes the pigment does not appear until shortly before a paroxysm. The presence of many bodies containing a considerable number of grains of pigment is generally indicative of an impending paroxysm. The pigment granules are at first very minute and few, and may be readily overlooked. The granules of pigment increase in number and size, but it is one of the characteristics of the æstivo-autumnal amœbæ that the formation of pigment is, as a rule, scanty and in fine grains. Often only one or two very fine pigment granules are seen in the periphery or on the inner edge of the refractive border of the hyaline bodies. Usually about six or seven granules of pigment are developed in the hyaline bodies. The pigment generally shows but little motion in contrast with that in the tertian amœbæ.

The æstivo-autumnal amœboid forms do not generally grow larger than one-quarter to one-third the diameter of the red blood-corpuscle, and they may remain smaller. The infected red corpuscles may appear otherwise normal. They do not become swollen and decolorized in this stage, as is the case in the tertian infections. On the other hand, they often become shrunken, creased, or otherwise deformed, and present a deep brassy color (*globuli rossi ottonati* of the Italian writers) (Plate II. Figs. 7, 16). Sometimes the hæmoglobin separates from a part or the whole of the outer part of the stroma of the corpuscle and collects around the enclosed hyaline body (Plate II. Fig. 13). These changes in the red corpuscles, which are particularly characteristic of the æstivo-autumnal variety, although not absolutely limited to it, are to be regarded as degenerative or necrobiotic. Marchiafava and Celli and some others have thought that the parasite within these profoundly altered corpuscles is also dead or incapable of further development. Bastianelli states that sporulation forms are not observed in the brassy corpuscles, but this statement is opposed to observations of Marchiafava and Bignami and others. The view that parasites within profoundly altered corpuscles are incapable of further development is by no means proven, and is opposed to the natural interpretation of many observations.

As the time for the onset of a paroxysm approaches, the hyaline bodies gradually cease their amœboid movements, assume a spherical or ovoid shape, become somewhat more refractive and homogeneous, and present a small collection of quiescent or but slightly moving pigment granules at about the centre or often near the periphery (Plate II. Figs. 13, 16, 17, 18). This pigment usually fuses into a single small, black, round or irregular mass or block (Plate II. Figs. 14, 15, 19–24), or there may be two such blocks.

These round, refractive bodies with pigment blocks or collections of pigment granules (*corpi con blocchetto*) are the presegmenting bodies, and when they are present the onset of a paroxysm, within at most a few hours, may generally be safely predicted. These bodies are much smaller than the corresponding forms of the quartan and tertian parasites. They do not generally exceed one-quarter or one-third of the size of the corpuscle, although they may be considerably larger. They are surrounded with hæmoglobin-containing substance of the corpuscle, which is often of a brassy color.

The next phase of development is that of sporulation, but the segmenting forms are found in the peripheral blood only most exceptionally, save in some pernicious cases, in which they may in rare instances be even abundant. Sacharoff observed in the Transcaucasus sporulating forms in the blood, and on this account, but apparently without sufficient reason, he regards this form as a special variety. For a few hours before and during the early stage of the paroxysm very few parasitic forms of any kind are to be found in the circulating blood, and at this period they may be entirely absent, in marked contrast to quartan infection. During this period the presence of pigmented leucocytes in the blood may aid in the diagnosis. In tertian infections an analogous condition is found, but not in the same degree. The disappearance of the parasites from the blood is believed by most authorities to be due to their deposition in internal organs, especially the spleen and the bone marrow, and is attributed to the profound changes in the red blood-corpuscles containing them, these changes rendering the corpuscles virtually foreign bodies which, like other foreign particles, are caught and retained especially in the spleen and the bone marrow.

Blood withdrawn by puncture of the spleen at this time will, with rare exceptions, show abundant intracorpuscular and free round bodies with central or peripheral pigment, and also segmenting forms. In certain cases segmenting forms are few in the spleen, but abundant in certain other internal organs, as has been shown by post-mortem examinations. These sporulating bodies are smaller than those of the quartan and tertian parasites, and occupy, as a rule, only a relatively small part of the corpuscle, which is always altered in appearance, being shrunken and brassy-colored or more frequently decolorized. They may appear to be free or may be actually free. In pernicious cases they are present in large, often enormous, numbers in the internal organs, especially in the spleen and bone marrow, and in some types of pernicious fever in the capillaries of the brain and in those of the intestinal mucosa. This varied distribution of the parasites in internal organs is in relation with the types of pernicious fever. The stage of sporulation occupies a rather long period and takes place in successive groups. This circumstance is believed to explain the long duration of the paroxysm in æstivo-autumnal fevers. In pernicious cases sporulation seems to be going on continually in the vascular areas of certain internal organs.

In æstivo-autumnal infections the process of sporulation is in general similar to that of the tertian parasite, but it is more irregular and variable and the spores are much smaller (Plate II. Figs. 25–28). The number of spores formed by a segmenting æstivo-autumnal organism is extremely variable. There may be not more than six to ten spores, or even fewer; often there are ten to twenty, and the number may exceed thirty. Some segmenting forms are much larger than others. Golgi has observed exceptionally very large ones containing as many as forty to fifty spores. There are slight differences often to be observed in the finer structure between the æstivo-autumnal spores and those of the quartan and tertian parasites, as will be described when we consider the intimate structure of the malarial parasites.

The young hyaline bodies of the new generation may be found in the blood in the early part of the paroxysm, but often they do not make their appearance until several hours after the beginning of the paroxysm or during its decline.

Not all of the æstivo-autumnal amœbæ develop pigment. Sporulation may occur in bodies, usually of small size, entirely devoid of pigment. As a rule in these cases both pigmented and unpigmented forms occur, but cases of æstivo-autumnal malaria have been observed, especially in tropical climates, in which only unpigmented bodies could be found at any stage of the fever before the appearance at a later period of crescentic bodies which always contain pigment.

As has already been mentioned (page 38) Grassi and Feletti regard the parasites which do not develop pigment as belonging to a distinct variety (*Hæmamœba immaculata*), but it is difficult to reconcile this view with the frequent association of pigmented and unpigmented forms, the frequent transitions from one to the other as regards the quantity of pigment developed, and the absence of any points of distinction other than the presence or absence of a variable, but generally small, amount of pigment. Still further researches, especially of the grave tropical malarias, may perhaps demonstrate the existence of a distinct unpigmented variety of the parasite.

There is considerable uncertainty as to the length of the cycle of development of the Hæmatozoön falciparum. This uncertainty is due to the manner of development of the parasite, usually in multiple groups, in the internal organs, the most characteristic reproductive phases being absent from the circulating blood. So far as one can judge from the study of these phases in connection with the different types of fever with which they may be associated, the length of the cycle of development may vary from twenty-four hours or less to forty-eight hours or more.

The Hæmatozoön falciparum may be associated with typical quotidian fever or with tertian fever, and in some of these cases the blood shows apparently only one group of organisms. As already mentioned, Marchiafava and Bignami believe that there are two distinct varieties or subvarieties of the æstivo-autumnal parasite, the one a true quotidian organism, with a cycle of twenty-four hours' duration, and the other their so-called malignant or summer-autumn tertian variety, with a cycle of forty-eight hours' duration; and this division has been accepted by some other authors. This distinction is based mainly upon the apparent duration of the cycle of development—in the quotidian about twenty-four hours, and in the malignant tertian forty-eight hours, more or less—but there are claimed to be other differences of a minor character relating to the pigmentation, the size, and the amœboid movements of the organisms.[1] The differential diagnosis is said to be possible only with the adult forms. The differential characters claimed to exist between the quotidian and the tertian varieties of the æstivo-autumnal parasite are, for the most part, only such as one would expect with a malarial parasite developing more rapidly in some cases than in others, and they, at least so far as at present formulated, scarcely suffice for a distinction into two well-defined varieties.

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[1] The following are the biological and morphological differences between the æstivo-autumnal quotidian and malignant tertian parasites, according to Marchiafava and Bignami (*On Summer-Autumn Malarial Fevers*, translation, p. 83, The New Sydenham Society, London, 1894): Duration of cycle of development in the quotidian, about twenty-four hours, in the summer tertian, forty-eight hours, more or less; in the quotidian sporulation on rare occasions is completed before the amœbæ have become pigmented—this is not observed in the summer tertian; the fine granules of pigment in the periphery of the summer tertian are sometimes endowed with oscillatory movements—this is not noticed in the quotidian; in the same relative stage of development the tertian amœba is usually larger than the quotidian, the adult pigmented tertian forms may be one-third of the size of the red blood-corpuscles, and the forms of segmentation may be one-half or two-thirds of it;

Thayer and Hewetson, while confirming Marchiafava and Bignami's recognition of quotidian and tertian fevers caused by the æstivo-autumnal parasite, emphasize the occurrence of intermediate types of fever, and in general the essential irregularity of the fevers caused by this organism. They were unable to distinguish any morphological or biological differences between the parasites associated with these various types of fever. Although unwilling to commit themselves to a positive conclusion, they are "inclined to believe that the irregularity of the febrile manifestations is due chiefly to the tendency on the part of the parasite to irregularities in the length of its cycle of development (this variability being dependent, perhaps, upon the malignity of the organism or upon the resistance of the individual affected); to the fact that the period of time required for the sporulation of one group of organisms is materially greater than in the regular infections, owing to the fact that the arrangement of the parasites in definite sharp groups, sporulating nearly at the same time, is much less distinct than in the tertian and quartan intermittents; to the fact that, frequently, organisms in all stages of development are present at one time, segmentation occurring almost continuously."[1]

Golgi also considers that Marchiafava and Bignami's division into quotidian and tertian æstivo-autumnal organisms is based upon insufficient evidence, and that the duration of the cycle of development of the æstivo-autumnal parasite is indeterminate, or at least has not as yet been accurately ascertained. This cycle is probably, he thinks, longer than is supposed by Marchiafava and Bignami. This form of parasite, according to Golgi, is characterized by the fact that it develops entirely in the internal organs, and that the forms, chiefly of the earlier stages of development, which appear in the circulation, although they are found there at certain periods of the disease in practically all cases, are, in a sense, accidentally present in this situation, being washed into the circulation from their foci of development, as nucleated red blood-corpuscles may be conveyed from the bone marrow into the blood current in certain anæmias. Golgi at first thought that the forms present in the circulation degenerate, but he does not now deny that they may lodge in internal organs and there develop into segmenting organisms. Marchiafava and Bignami with much reason vigorously contest Golgi's conception of the "accidental" nature of the presence of æstivo-autumnal organisms in the circulating blood, although they also believe that a large part of the parasites develop wholly in the internal organs, and

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in the tertian the amœboid movements are maintained longer, even in the adult pigmented forms, and the motion is more lively than in the quotidian during the pigmented phase; the duration of the non-pigmented amœboid phase in the tertian is relatively long and may exceed twenty-four hours; the young forms of the new generation in the tertian usually appear in the blood several hours after the beginning of the paroxysm, which is much later than in the quotidian.

[1] *Op. cit.*, pp. 151, 153.

that sporulation occurs only most exceptionally in the circulating blood.

The two most important and original points in Golgi's doctrine concerning the æstivo-autumnal parasite are that groups of the parasitic organisms are variously distributed in vascular areas in the internal organs, and there develop more or less independently of each other, "with relative stability," and that a large number of the organisms develop within leucocytes, endothelial cells, and other tissue-cells. All phases of development, according to Golgi, are found within these cells. The spleen and the bone marrow are situations preferred by the parasite, but the capillaries of the liver, of the brain, of the lungs, of the intestinal mucosa, may also contain them enclosed within cells.

A. Monti[1] has recently described these intracellular forms in pernicious malaria, and he confirms the observation of many others that cells containing parasites frequently degenerate and die. He finds apparently intact parasites not infrequently within cells, particularly endothelial cells.

It is contended by Marchiafava, Bignami, and Bastianelli that the intracellular inclusions of the parasite, upon which Golgi bases his doctrine, are simply the well-known phagocytic phenomena, and that such enclosed parasites belong chiefly to the later stages of development (presegmenting and segmenting bodies and spores), and that, instead of developing, they degenerate within the cells. The young amœboid bodies, which, according to Golgi's doctrine, should be frequently found within cells, they found only with comparative infrequency within phagocytes, and then almost always within their corpuscular hosts, which had been swallowed by cells. They admit the possibility of some development of intracorpuscular parasites which have been taken up by phagocytes, but not of free parasites within cells.

As with the other varieties of the malarial parasite, the æstivo-autumnal do not all mature and segment. Extracorpuscular forms are common, and it is more particularly these forms, deprived of the protective covering of the red blood-corpuscles, which degenerate. Adult and presegmenting bodies and bodies of the crescentic phase frequently become swollen and pale or vacuolated or fragmented, or throw off buds, or present other degenerative changes which have been described.

Phagocytism in the æstivo-autumnal, as in all malarial infections, is a phenomenon of much importance, as will be subsequently explained.

The frequency with which two or more groups of parasites in different stages of development are found in æstivo-autumnal infections has already been repeatedly emphasized. Marchiafava and Bignami believe that even in the pernicious fevers there are not generally present more than two groups of the æstivo-autumnal parasite, and that the short cycle of development and the prolonged period of sporulation suffice to explain the simultaneous presence of parasites in notably different stages of development. Combined infections with the æstivo-autumnal parasite and one of the other varieties occasionally occur.

It is important to bear in mind the discrepancy which characterizes æstivo-autumnal malaria between the number of parasites in the blood and the number in the internal organs. In the majority of cases the more severe the infection the greater the number of parasites found in the circulating blood, but there are so many exceptions to this that the number of parasites in the blood cannot be considered a trustworthy index of the number within the body. Pernicious cases have been repeatedly observed where the splenic blood examined during life or the internal organs examined after death contained enormous numbers of æstivo-autumnal parasites, although the blood of the finger showed very few. The organisms may be few even in the spleen when they are abundant in the cerebral capillaries or in some other situation. As will be explained subsequently, the varying symptoms and types of pernicious malaria can be explained in large part by the varying distribution of the parasites in internal organs.

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[1] A. Monti: *Bollettino della Società medico-chirurgica di Pavia*, 1895.

It is evident from the description which has been given of the æstivo-autumnal parasite that this variety is characterized especially by its great activity in multiplication, and it will appear from the consideration of the clinical features of the infections caused by this parasite that other most important characteristics are its virulence, greater than that of other varieties, and its greater resistance to quinine.

There is a group of bodies of crescentic, fusiform, oval, or round shape, presenting certain common and peculiar characters, which develop only from the Hæmatozoön falciparum. The crescents are the most typical of these bodies, which may be designated, therefore, as bodies of the crescentic (or semilunar) phase or group. They merit special consideration.

Bodies of the Crescentic Group.—When a malarial fever caused by the Hæmatozoön falciparum has lasted a week or more bodies of the crescentic or semilunar phase are likely to appear in the blood. They are very rarely found in the blood in the latter part of the first week. If the fever is treated with sufficient doses of quinine during the early part of the first week, crescents do not appear, but the administration of quinine after the fever has lasted much longer than a week does not prevent their appearance. They may persist in the blood two weeks or more after all other forms of the parasite have disappeared. In such cases they are often unassociated with any febrile manifestations or any symptoms which can be definitely referred to their presence. If a relapse of the fever occurs, then the young hyaline bodies already described are always present. The crescents themselves are very resistant to the action of quinine. Councilman in 1887 called attention to the occurrence of crescentic bodies as characteristic of the irregular and remittent forms of malarial fever and malarial cachexia.

There was for a time much doubt as to the origin of the crescents, but Marchiafava and Celli's demonstration in 1886 of their intracorpuscular development has been abundantly confirmed by the later studies of Canalis, Bastianelli and Bignami, and others. The early intracorpuscular stages of development of the bodies of the crescentic group are rarely seen in the circulating blood, except in certain pernicious cases, but they can often be found in the splenic blood. Bastianelli and Bignami have found these early phases so abundantly in the bone marrow that they consider that they develop by preference in this situation.

Certain of the intracorpuscular spherical forms of the Hæmatozoön falciparum with collected pigment granules, instead of continuing their regular cycle of development into segmenting forms, are transformed into the young bodies of the semilunar phase. This transformation takes place only after a number of febrile paroxysms; that is to say, only after the parasite has repeatedly passed through its regular sporulating cycle of development.

The young bodies of the crescentic group occupy perhaps one-quarter of the red corpuscle. Their shape is round, oval, or fusiform. They present a characteristic homogeneous, refractive appearance, being more refractive than the presegmenting bodies with central blocks of pigment. They contain dark pigment, usually in the shape of fine rods, sometimes collected in a mass, but oftener irregularly distributed. In the fusiform bodies the pigment is often arranged along the longitudinal axis of the spindle. The hæmoglobin is frequently retracted into a denser stratum around the bodies. These bodies increase in size without a correspondingly large increase in the amount of pigment, and, as will be explained later, without a corresponding increase in their chromatic or staining substance—a point which distinguishes the direction of crescentic development from that of the regular sporulating development.

It is some time after these young semilunar bodies have begun to form in the bone marrow and spleen before the adult crescents appear in the circulating blood. These completely developed typical crescents are on the average 8–10 μ long, and in the middle 2–3 μ broad (Plate II. Figs. 31, 32, 33). They do not often exceed in length one and a quarter or one and a half times the diameter of a red corpuscle. They present a characteristic, homogeneous, refractive appearance. An outer double-contoured border can sometimes be seen, especially after treatment with certain reagents, and this is interpreted by Laveran, Mannaberg, and many authors as evidence of a distinct enveloping membrane; but the weight of evidence is opposed to the view that the crescents, any more than any other form of the malarial parasite, possess a membrane other than that which pertains to the enveloping red corpuscle. The outer refractive margin of the crescents, as pointed out by Antolisei and Angelini—who interpret it as a cuticular envelope derived from the red blood-corpuscle—may be slightly colored by hæmoglobin, and it may show evidence of this presence of blood coloring matter by the staining with eosin. On the typical crescent-shaped forms a fine line can often be seen stretching like a bow across the concavity, its attachment at each end being within the extremities of the horns. This line is derived from the red blood-corpuscle within which the crescent has developed, and represents the outer contour of the partly or completely decolorized corpuscle. This contour of the corpuscle can sometimes be detected also on the convexity of the crescent, and parts of the corpuscle still containing hæmoglobin may occasionally be seen on the margin of the crescent, or the whole crescent may be surrounded with hæmoglobin-containing corpuscular substance (Plate II. Fig. 29). Similar evidences of the partly or completely decolorized enveloping blood-corpuscle can frequently be seen on the margin of the round and oval bodies (Plate II. Figs. 34, 35, 36, 38, 39).

Bodies of the crescentic group are always pigmented. The pigment is very dark in color, often black, and mostly in fine rods. In the typical crescents the pigment, which is without movement and in fine rods and grains, is usually collected in the middle, sometimes in a single clump or in two clumps. often in a coronal shape. Mannaberg emphasizes the frequency with which the pigment is arranged in two adjacent clumps near the centre, presenting a figure-of-8 shape. In the immature crescents the pigment is often scattered, or is arranged longitudinally, as it often is in the fusiform bodies. The amount of pigment varies; it is often considerable. In certain pernicious fevers young crescents with scattered pigment may be abundant in the blood. In the oval and round bodies the pigment is usually concentrated in the centre, often in the form of a circle, but it may be distributed throughout the body. Ovoid, round, and fusiform bodies may be changed into typical crescents, and, on the other hand, crescents may change into fusiform, oval, and round bodies. The appearance of a fusiform or ovoid body may be presented when a crescent is seen from the convex side.

From the round bodies flagellate forms may develop in the manner already described (Plate II. Figs. 42, 43, 44). The æstivo-autumnal flagellate bodies develop only from round bodies of the crescentic group. They are smaller than the tertian flagellates, resembling rather the quartan. The process of transformation of crescentic bodies into oval and round forms, and the development of flagella from the latter, can sometimes be observed in studying the fresh blood microscopically. Councilman once observed a rapid undulatory movement of a body presenting the general appearance of a crescent.

Crescents and the other bodies belonging to the same phase not infrequently become vacuolated or contain or throw off from the margin little hyaline balls (pseudo-gemmation), or disintegrate or present other degenerative changes (Plate II. Figs. 34, 41, 40). Danilewsky has observed crescents of unusually large size, as much as 20–22 μ long and 4–6 μ broad.

The biological significance of the crescents is unknown. These bodies do not belong to the regular sporulating cycle of development of the parasite, and there is no positive proof of their capacity for further development.

Dr. Thayer in a personal communication to the writer reports a valuable experiment made by himself which demonstrates the incapacity of crescents when inoculated into the blood of healthy individuals to develop or to cause any symptoms. The blood was taken from a patient who had had acute æstivo-autumnal fever, which was arrested by administration of quinine. Crescents persisted in the blood. For seven days the blood was examined without finding hyaline bodies or any form of the malarial parasite other than crescents. Seven days after the disappearance of the hyaline bodies a hypodermic syringeful of blood containing crescents in considerable number was withdrawn from the median basilic vein of the patient and immediately injected into the corresponding vein of a healthy man. No elevation of temperature or other symptoms followed the injection, nor did crescents or any parasitic forms make their appearance in the blood, which was examined daily for two weeks and at intervals for over a month. In the inoculation experiments of Gualdi and Antolisei and others in which it is stated that the blood contained only crescents and infection with the Hæmatozoön falciparum followed in the inoculated individual, it is probable that hyaline bodies were present in the blood used for the inoculation in such small number that they escaped detection.

The following are the principal views which have been advanced regarding the interpretation of the crescents:

1. Laveran regards the crescentic bodies as encysted forms from which the flagella develop. There is no proof that these bodies are encysted.

2. Canalis and Antolisei and Angelini believe that they have found evidences of sporulation in the crescents and the ovoid and round bodies belonging to the crescentic phase. Grassi and Feletti and Sacharoff likewise believe that these bodies may sporulate. Golgi considers them capable of reproductive development in long cycles, and brings them into special relation with relapses and with fevers of long intervals. Most observers have been unable to find genuine sporulation or other evidences of reproduction in these bodies.

3. Grassi and Feletti consider that the crescents belong to a separate species which they call *Laverania,* and of which they represent a regular phase of development. The sporulating hyaline bodies with which the crescents are usually associated constitute, according to these writers, different species. This view is not generally accepted, and is opposed to the observed facts.

4. Mannaberg regards the crescents as encysted syzygies formed by conjugation of two æstivo-autumnal parasites and capable of reproduction by segmentation. His view is unconfirmed by any other observer, and is improbable. It fails to explain the ovoid and round bodies which belong to the same phase of development, and it cannot be reconciled with the appearances noted in the steps of development of the crescents, as has been shown by Bastianelli and Bignami.

5. Councilman suggests that the crescents may be of the nature of spores. Several authors have called attention to a resemblance between these bodies and the falciform spores of coccidia, but there are such essential differences between the two that the apparent resemblance is only of the most superficial character.

6. Bastianelli and Bignami have described the crescents as deviate and sterile forms. This has been interpreted to mean that they regard the crescents as degenerative forms—a view held by Kruse and some others—but in their latest publication[1] they suggest that these bodies are a rudimentary phase of a second developmental cycle which cannot be completed within the human body, but requires for its continuation some new environment in the outer world. They call attention to the occurrence of two cycles of development in several unicellular parasites, especially the coccidia, which, after passing through several generations in their ordinary parasitic life, enter upon forms belonging to a second cycle. The forms of this second cycle remain sterile, degenerate, and die, unless the parasite can escape from its host and find its appropriate new conditions of life. Manson independently also has advanced the hypothesis that the crescents are intended for the continuance of the life of the species in the external world. It has already been mentioned that a similar view has been suggested also regarding the significance

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[1] Bastianelli and Bignami: "Studi sulla Infezione Malarica," *Bullettino della R. Accademia Medica di Roma,* Anno XX., 1893–94.

of the flagellate bodies, and that Manson believes that the mosquito may serve as the host for this second cycle of development.

DIFFERENTIAL DIAGNOSIS OF THE VARIETIES OF THE MALARIAL PARASITE.

An inexperienced observer may possibly mistake for the unpigmented intracorpuscular hyaline forms of the malarial parasite the vacuoles which occasionally are present within red blood-corpuscles or the clear spots which may result from certain deformities in the shape of the corpuscles. These vacuoles and clear spots may be distinguished in the fresh specimen by their sharp outlines, the absence of amœboid changes of shape, and a difference in refraction often suggestive of an empty space or hole, and which can be described less readily than it can be appreciated by actual observation. The absence of definite staining readily distinguishes these vacuoles from the hyaline bodies of the parasite in stained specimens.

There are occasionally seen in red corpuscles in stained specimens of the blood, especially in anæmic conditions, small stained dots which do not bear much resemblance to forms of the malarial parasite, but which should be known to the observer in order to avoid the possibility of mistake. They are believed by some to be the result of degenerative changes in the corpuscles, and by others to be remnants of nuclear chromatin derived from the originally nucleated condition of the red corpuscle.

Blood-plates can be mistaken only for free spores or very small extracorpuscular hyaline bodies. In general no attention should be paid as regards diagnosis to bodies free in the plasma which resemble blood-plates. In fresh specimens it is practically impossible to diagnose free spores with any certainty. Clumps of blood-plates have been mistaken for sporulating bodies, but they can be readily distinguished from the latter by the absence of pigment.

For the sake of convenience the principal characters which enable us to distinguish each of the three varieties of the malarial parasite, and which have already been described in detail, will here be summarized. For modifications and amplification of these general statements the reader must consult the detailed descriptions already given.

1. DURATION OF THE CYCLE OF DEVELOPMENT.—In the quartan parasite, seventy-two hours; in the tertian, forty-eight hours; in the æstivo-autumnal, irregular, varying from twenty-four hours to forty-eight hours.

2. AMŒBOID HYALINE BODIES.—In their earliest stages often indistinguishable from each other. Later, those of the quartan parasite, sharply outlined, somewhat refractive, sluggishly amœboid, with development of dark brown or black, relatively coarse pigment granules, which have but little motion. Amœboid movements cease in a relatively early stage of development of the pigmented hyaline body.

Those of the tertian parasite, pale and indistinct, actively amœboid, with development of reddish-brown, actively motile, relatively fine pigment granules, which tend to accumulate in the bulbous swellings at the extremities of the delicate branching pseudopodia. Amœboid movements continue in late stages of development of the pigmented amœbæ.

Those of the æstivo-autumnal parasite, small, somewhat refractive, in repose ring-shaped, actively amœboid, with development of a few very fine dark reddish-brown or black, only slightly motile, pigment granules, or sometimes without pigment throughout all phases of the sporulating cycle of development.

3. Fully Developed Hyaline Bodies.—Those of the quartan parasite are somewhat smaller in size than the normal red blood-corpuscle, and are usually surrounded by a border of the colored refractive substance of the enveloping red blood-corpuscle.

Those of the tertian parasite attain the full size of a normal red blood-corpuscle and lie in swollen decolorized red blood-corpuscles. Swollen, extracorpuscular, transparent bodies with dancing pigment granules are common.

Those of the æstivo-autumnal parasite do not generally exceed one-quarter to one-third the size of the red blood-corpuscle. The enveloping corpuscle is often shrunken and brassy. They contain much less pigment than the quartan and tertian forms, and sometimes none at all.

4. Presegmenting Bodies.—In the process of collection of the pigment into a mass or block in the centre or excentrically the pigment granules often assume a more regular stellate arrangement in the quartan than in the tertian forms. The differential points between the three varieties in this stage relate to the same differences in size, in the amount of pigment, and in the condition of the infected corpuscle as have been mentioned under the preceding heading. The presence in the blood of quartan and tertian presegmenting bodies is associated with that of sporulating forms, whereas with the æstivo-autumnal presegmenting bodies sporulating forms are almost always missed in the circulating blood.

5. Sporulating Bodies.—Those of the quartan parasite in equal proportion in the peripheral and the splenic blood. They are somewhat smaller than the red corpuscles, and present typical rosette forms with a division into six to twelve ovoid or pyriform segments, each segment becoming an oval or round spore containing a bright nucleiform dot.

Those of the tertian parasite are more numerous in the splenic than in the peripheral blood. They are as large as the red blood-corpuscle, and present less regularity in segmentation than the quartan parasite. They segment usually into from fourteen to twenty spores, which are a little smaller and with less distinct nucleiform dot than those of the quartan organism.

Those of the æstivo-autumnal parasite are found only most exceptionally in the circulating blood in ordinary cases. They are abundant in certain internal organs, including, as a rule, the spleen. They do not generally exceed one-third to one-half the size of the red blood-corpuscle. They segment irregularly, the number of spores being sometimes six to ten, sometimes ten to twenty or even more. The spores are smaller than those of the quartan and the tertian parasites. The stage of sporulation is a prolonged one.

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somewhat shrunken and deeper in color in the quartan infections; swollen and decolorized in the tertian; and shrunken and brassy, sometimes with retraction of hæmoglobin from the outer part of the corpuscle, in the æstivo-autumnal.

7. CRESCENTIC BODIES.—Crescents and bodies of the crescentic phase appear only in infections with the æstivo-autumnal parasite.

8. PIGMENTED LEUCOCYTES.—Most abundant during and shortly after the paroxysm, they usually disappear during the period of apyrexia in quartan and tertian infections, whereas it is not uncommon to find them in all periods of æstivo-autumnal infections.

THE INTIMATE STRUCTURE OF THE MALARIAL PARASITE.

The first systematic study of the finer structure of the malarial parasite was made by Celli and Guarnieri (1888–89). This was followed by similar investigations by Grassi and Feletti, Romanowsky, Sacharoff, Mannaberg, Antolisei, and Bastianelli and Bignami. The small size and the but slightly differentiated appearance of most forms of the parasite, and the difficulty of obtaining clear differential stainings, obscure the insight into their intimate structure.

Little detail of structure can be made out in unstained specimens. The substance of the parasite presents in general a homogeneous, colorless, hyaline appearance. In the amœboid hyaline bodies of the quartan and tertian parasites, particularly in the larger forms, an area of variable size in the centre, or more frequently excentrically placed, may sometimes be differentiated by its clear, pale appearance from the more refractive outer zone. This area corresponds to the unstained structure interpreted by many observers as the nucleus in stained specimens. Occasionally two or more such clear spaces can be seen. Sometimes in the larger amœboid and the mature forms a finely granular appearance of the protoplasm can be detected. It is particularly characteristic of the æstivo-autumnal parasite that the young intracorpuscular hyaline bodies show, when at rest, a clear space surrounded by a ring of protoplasm, usually thin and delicate on one side and thicker on the other. This clear space appears unstained on stained specimens. The mature forms in which the pigment has collected into one or more clumps appear uniform in structure in fresh specimens, or may perhaps present a slightly granular appearance. Within the spores, especially distinctly in those of the quartan parasite, a bright body can often be distinguished, which represents the nucleus or a nucleiform material.

The methods for staining the parasites will be described under *Diagnosis*, page 139. These methods are useful, not only for the study of the finer structure, but also for the ready detection of the unpigmented young hyaline forms, particularly of the æstivo-autumnal parasites, which may, without very careful observation, escape recognition on fresh specimens, whereas the presence of pigment at once attracts attention in the fresh specimens to the other parasitic forms.

On suitably stained specimens the intracorpuscular young hyaline bodies show a stained outer part, an unstained, usually excentrically placed, internal part, and one or more deeply stained round or elongated particles situated, as a rule, near the border of the stained and unstained parts. The constant unstained part is not to be confounded with vacuoles which may occasionally be present. There have been various interpretations of the structures thus differentiated. Celli and Guarnieri designated the stained part as ectoplasm and the unstained part as endoplasm. The deeply staining particles they interpreted as the beginning differentiation of a nucleus, which they thought they could recognize in larger forms as a definite, stained or pale body within the endoplasm. Grassi and Feletti do not recognize a division of the protoplasm into ectoplasm and endoplasm, and in this they are followed by most observers. The clear unstained part they interpret as a relatively large, vesicular nucleus, and the deeply staining particles as nucleoli from which may proceed a delicate reticulum of chromatin connecting them with the nuclear membrane which they assume to exist. The rest of the bladder-like nucleus is filled with clear nuclear juice. Although not all of these details in the structure of the nucleus, such as the membrane and the reticulum, have been observed by subsequent investigators, Grassi and Feletti's interpretation of the unstained part as a nucleus and of the deeply staining particle as a nucleolus or a concentration of nuclear chromatin has been adopted by Celli and Sanfelice, Romanowsky, Sacharoff, and Mannaberg, and has been widely accepted.

Bastianelli and Bignami, while not denying that this interpretation is applicable to the quartan and tertian amœbæ, adopt a different view as to the structure of the æstivo-autumnal amœbæ, which they have studied with great care. They differentiate in the latter an outer colored, chromatic cytoplasm in the form of a stained ring, usually thicker on one side, and an inner uncolored, achromatic cytoplasm, which is all of the clear part enclosed by the ring. The deeply staining chromatic particle they find in the chromatic and not in the achromatic cytoplasm. Often there are two particles, each at opposite points in the ring. This particle is the only representative of nuclear material in the parasite, and they interpret it as fulfilling the functions of a nucleus. They consider that the rapidity of development and multiplication of these æstivo-autumnal parasites prevents the formation of a definite nucleus in a resting stage, such as is described for the quartan and tertian forms.

According to Grassi and Feletti and Romanowsky, the nucleus and nucleolus can be found in all stages of the regular cycle of development of the parasite. The nucleus divides directly—or, according to Romanowsky, by karyokinesis—to form multiple nuclei just before sporulation, each nucleus then entering into the structure of a spore.

The evidence, however, is in favor of the view that at a certain stage of development the nucleus and the nucleolus disappear as differentiated structures, the latter to reappear in multiple form shortly before sporulation. Mannaberg was the first to demonstrate this clearly in his studies of the structure of the tertian parasite. He observed that as the amœboid bodies approach their mature form, and then become the presegmenting bodies, the deeply staining particle (nucleolus) disappears, and later the clear, previously unstained part (nucleus) stains diffusely, so that there is in this stage no definite differentiation of structure in the parasite, although the outer part, as a rule, stains more deeply than the central part. He, however, speaks of the outer part, which contains pigment granules, as the "plasma part," and the inner part, into which the pigment does not penetrate, as the "nuclear part." He attributes the deeper and more diffused staining of the parasite in this stage to the solution of nuclear chromatin into the protoplasm. The first evidence of sporulation on stained specimens is furnished by the appearance of numerous small, deeply staining granules of chromatin in the periphery of the protoplasm. These are the forming nucleoli, which increase in size, and around each the general protoplasmic substance, during the process of segmentation, divides, so that each segment or spore is a cell composed of a nucleiform, deeply staining body surrounded by its protoplasmic envelope. In the quartan and tertian spores a clear unstained part later is usually differentiated around the chromatin granule, and the nucleus now resembles that seen in the young amœboid hyaline bodies within the red corpuscle.

Bastianelli and Bignami likewise demonstrated the disappearance of the deeply staining nucleiform body in the forms of the æstivo-autumnal parasite containing collected pigment (presegmenting bodies), and soon afterward the appearance of diffuse staining in the previously achromatic cytoplasm, so that in this stage no sharp differentiation of structure can be made out within the parasite, which is richer in chromatic material than before the disappearance of the nucleiform body. The first sign of sporulation is the formation of multiple nucleiform chromatin granules in the periphery and the development of spores proceeds in the manner already described, save that the æstivo-autumnal spores are composed only of the deeply staining nucleiform body immediately surrounded by cytoplasm. The presence of the small, clear, unstained part, which with the chromatin particle is interpreted as the nucleus, often seen in the tertian and quartan spores, is rarely observed in the æstivo-autumnal spores.

It is evident from this description that the spores of the malarial parasite possess a definite structure, a most important feature being the presence of a deeply staining body which serves the function of a nucleus. The recognition of this structure renders it possible to distinguish from genuine spores the various pseudospores which have been at times erroneously interpreted as phases of reproduction of the parasite, and which belong to the category of degenerative forms. Although Antolisei has described a double contour, which he interprets as a membrane, about the spores, this observation has not been confirmed, and the spores are to be regarded as naked, thus belonging to the class of gymnospores. Some have objected to the designation of these segments as spores, but this nomenclature is in accordance with that employed by zoölogists for similar bodies formed in a like manner in certain other unicellular organisms.

It is evident from the preceding description that investigators are not wholly agreed as to what structure in the malarial parasite shall be called the nucleus, some applying this name to an unstained part containing the deeply staining chromatin particle, others regarding the chromatin granule itself as the only representative of the nucleus. There is, however, general agreement that this deeply staining particle or body is an essential constituent of the nucleus, and that the presence of a nucleus or of a nucleiform body in the parasite has been demonstrated. This demonstration fulfils the important biological condition that something performing the functions of a nucleus belongs to every cell capable of reproduction, and it has served to remove any lingering doubt which may have been entertained as to the recognition of these bodies as parasitic organisms.

It is interesting to note that during the regular cycle of development there is a continual increase in the amount of staining or chromatic substance from the small hyaline body to the sporulating bodies, and that the cell becomes multinucleated just before segmentation occurs. As the chromatic substance is to be regarded as endowed with especial functional activity, these changes are highly significant.

The mature crescents, as a rule, stain feebly and diffusely, or often only at the poles, and perhaps also along the margin. Near the middle one or two deeply stained granules, often covered up by the pigment, may be present, but they are not constant. Mannaberg finds often a narrow stained band in which are two or more deeply stained granules, stretching across the middle of the crescent. Bastianelli and Bignami find that the young developing bodies of the crescentic phase stain diffusely and less intensely than the bodies with a central block of pigment which develop into segmenting forms. Whereas in the forms of the parasite which develop into sporulating bodies there is a continual increase in the chromatic substance as the bodies continue to develop, in the development of the semilunar bodies there is no correspondingly large increase of staining substance. With rare exceptions these observers found no chromatin granules in these developing crescentic bodies, nor did they ever find in any body of this group those changes of structure, such as the appearance of several chromatin granules, which indicate sporulation.

Laveran, Celli and Guarnieri, and, with especial emphasis, Mannaberg, consider that the crescents are enveloped in a double contoured membrane. A number of other observers have also adopted this view. We do not consider that any definite membrane, which can be regarded as a part of the parasite itself, has been satisfactorily demonstrated around the crescents or around any form of the malarial parasite. A double contour can sometimes, but not regularly, be seen in the periphery of the crescents, but this alone cannot be considered as proof of the existence of a membrane. The manner in which little hyaline pieces (pseudo-gemmation) can sometimes be seen to form at the margin of the crescentic bodies speaks against the presence of an actual membrane.

THE MALARIAL PIGMENT.

The question as to the origin of the malarial pigment, which was so long discussed without conclusive result before the discovery of the malarial parasite, has been definitely settled by this discovery. The pigment is formed by the parasite out of the hæmoglobin of the blood-corpuscles by what may be regarded as a process of digestion. The pigment occurs in the form of little granules, which may be fine or coarse, and of distinct rods and spicules, which may be as much as 1 μ long. Such rods often present a certain superficial resemblance to deeply stained bacilli. The pigment may occur in the form of extremely fine dust-like particles not easy to detect. It may be fused into black blocks. The color varies from a yellowish-brown or rusty, reddish-brown to black. Laveran speaks of fire-red and even light-blue pigment, and Rosenbach observed a greenish hue of the pigment. The malarial pigment is somewhat loosely ranked by pathologists among the melanin pigments. The differences in the characters of the pigment belonging to the different varieties of the malarial parasite have already been sufficiently described. The deposition of the pigment in the various organs will be described under the *Pathological Anatomy*.

Since the examinations of malarial pigment by Meckel and by Frerichs it has been known that concentrated sulphuric acid and hydrochloric acid do not alter it, and that it disappears upon the addition of strong alkalies and of chloride of lime. Kiener observed that the pigment is dissolved by ammonium sulphide.

The demonstration of the origin of the malarial pigment from the blood coloring matter at once raised the question whether, like many pigments of hæmatogenous origin, it contains iron demonstrable by our micro-chemical tests. A statement by Perls as long ago as 1867, that pigments in the spleen of intermittent fever respond to the test for iron, has given rise to much confusion. It is not wholly clear that Perls examined the malarial pigment, but, if he did, there can be no doubt that he mistook for the true malarial pigment other pigments which are abundantly present in certain organs of those dead of malaria, and which respond to the chemical tests for iron (hæmosiderin). It has been shown by Neumann, Bignami, Stieda, Dock, and others that the pigment formed directly by the malarial parasite does not contain iron in a combination which will respond to our ordinary micro-chemical tests for this element. This, of course, does not prove that it may not contain iron in some combination, such as that in hæmoglobin, which cannot be demonstrated by our micro-chemical reactions. As has been pointed out by the writers named, the organs of those dead of malaria, particularly the spleen, the liver, and the bone marrow, contain a large amount of hæmosiderin, the presence of which is doubtless to be explained by the extensive destruction of red blood-corpuscles in malaria. There is no evidence that hæmosiderin is formed directly by the malarial parasite. Marchiafava (1889), however, has advanced the hypothesis that the black pigment may be formed not only within the malarial parasites, but also within the leucocytes out of red corpuscles altered by the action of the parasite. He thus explains the intense melanosis of the spleen, liver, and bone marrow in certain æstivo-autumnal pernicious infections where the parasites appear only slightly pigmented. Bignami[1] comes also to the conclusion, from his extensive examinations of melanotic organs in malaria, that the black pigment without micro-chemical iron reaction may have this double origin, being formed either within the malarial parasite without an intermediate hæmosiderin stage or within cells out of hæmosiderin derived from destroyed red corpuscles. The objection to this conclusion of Bignami is that hæmosiderin is found in the liver, spleen, and bone marrow very commonly in anæmias, but that the black pigment, without micro-chemical iron reaction, which characterizes malarial infections, does not appear under these conditions. It is possible that the malarial parasite may produce some chemical change in the substance of the red blood-corpuscle which permits the transformation of the specifically altered hæmoglobin into black malarial pigment within certain cells of the body. This, however, is a pure hypothesis.

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[1] *Bullettino della Reale Accademia Medica di Roma*, Anno xix. fasc. ii. p 230, 1893.

PHAGOCYTISM.

The presence of malarial pigment in leucocytes and other cells has long been known. Since the observation of phagocytic phenomena in malaria by Laveran, Marchiafava and Celli, and Metchnikoff, important studies of this subject have been made, especially by Guarnieri, Golgi, Bastianelli, and Marchiafava and Bignami.[1] These investigations have shown that phagocytosis is a common and important phenomenon in malaria, although there is much difference of opinion as to the interpretation of some of the observed facts. Some assign to the phagocytes no higher rôle than that of scavengers charged with the collection and removal of the pigment and débris resulting from the activities of the malarial parasites and from the death and disintegration of the parasites themselves. The amount of slag which is produced in severe cases of malaria in the form of pigment, dead and disintegrating red blood-corpuscles, and degenerated and broken-up parasites is so large that even this office of scavengers becomes an important one. But Metchnikoff, Golgi, and some others believe that the phagocytes devour large numbers of intact, healthy parasites in certain phases of their development, and that in this contest between cell and parasite is to be found the most important agency for the defence of the body. The arguments for and against this latter conception are essentially similar to those which are adduced as to the phagocytic theory in bacterial infections, the main difficulty being to determine to what extent fully active and virulent parasites are taken up and destroyed by phagocytes, and, even admitting the occurrence of this mode of disposal of the parasites, whether or not it is the most essential and the predominant factor in their destruction. That malarial parasites, as well as bacteria, may perish in the blood plasma without incorporation within cells cannot be doubted, as we have direct observations demonstrating this.

The cells which assume the functions of phagocytes in malaria are the leucocytes, the endothelial cells of the walls of the bloodvessels, and large cells, found especially in the spleen, the bone marrow, and the liver, and called by Metchnikoff "macrophages." Of the leucocytes the large mononuclear, the polymorphonuclear, and the transitional forms act as phagocytes. The small lymphocytes and the eosinophils have never been observed to contain pigment or débris in malaria. Of the leucocytes it is the large mononuclear forms which are the most active and important phagocytes within the body in malaria, but, as has been pointed out by Thayer and Hewetson, the polymorphonuclear leucocytes are the ones which can be observed to be active in the fresh blood during examination under the microscope. It is the latter which pick up the pigment and the extracorpuscular and degenerated parasites, and which attack the flagellated bodies in the fresh blood withdrawn from the body, so that there may be a notable difference between the blood examined immediataly after its withdrawal from the body and that examined at a later period as regards the number of polymorphonuclear leucocytes containing foreign elements. Endothelial cells containing pigment, parasites, or fragments of parasites or of red corpuscles are rarely seen in the circulating blood withdrawn for microscopical examination; but the study of microscopical sections of organs of those dead of malarial infections shows that the endothelial cells lining the capillaries and small bloodvessels, especially those of the spleen, bone marrow, and liver, in certain cases also of the brain, intestine, and other parts, manifest extensive phagocytic activities. So too the macrophages, although they have repeatedly been found in the circulating blood, are met with chiefly in the splenic blood and in the microscopical examination of organs of those dead of malaria. These macrophages, which may attain an enormous size and are frequently destitute of nuclei, and therefore necrotic, are mononuclear cells derived probably in part from mononuclear leucocytes and certain fixed cells of the pulp of the spleen and bone marrow. Their contents may be varied, consisting sometimes within one cell of pigment, intact or degenerated parasites, and red blood-corpuscles and entire smaller phagocytes. Dock has counted as many as twenty parasites within one phagocyte in the spleen. Under *Pathological Anatomy* will be described the appearances of these various phagocytes as seen in sections of the different organs of the body.

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[1] Especially valuable are the articles of Golgi, "Il fagocitismo nell' infezione malarica," *Riforma Medica*, 1888, and of Bastianelli, "I leucociti nell' infezione malarica," *Bull. della R. Accademia Medica di Roma*, 1892.

The foreign elements which are found within these phagocytes in malaria are—(1) malarial pigment; (2) yellowish or reddish-yellow pigment derived directly from disintegrated red corpuscles (hæmosiderin); (3) red corpuscles, sometimes intact, but usually more or less altered and fragmented; (4) malarial parasites, either free or enclosed within red corpuscles, which are usually altered, such parasites appearing sometimes intact, often degenerated and fragmented; (5) particles which are probably often derived from the disintegration of parasites, but which do not present appearances sufficiently characteristic to enable one to determine their origin. It has already been mentioned that a phagocyte may be enclosed by a macrophage. Leucocytes either with or without pigment may be thus enclosed. As phagocytes and other cells often degenerate and become necrotic and disintegrated in malaria, it is evident that from this source may be derived material for inclusion within living cells.

First in order of frequency are phagocytes containing malarial pigment. In the examination of malarial blood obtained from the peripheral circulation the only form of phagocyte which is to be seen with any frequency in the perfectly fresh specimen is the melaniferous leucocyte. Leucocytes containing clearly recognizable parasites are rarely, if ever, seen in the freshly drawn specimen of peripheral blood. Macrophages containing definite parasitic forms may occasionally be found in this situation. Both mononuclear and polymorphonuclear leucocytes may contain the pigment, but in the perfectly fresh specimen the former preponderate. The pigment is found most frequently in the form of blocks and coarse granules, corresponding to that set free by the process of sporulation, but sometimes the pigment within the leucocytes is in fine rods and grains, such as belong to the earlier stages of development of the parasite. The inference is a probable one that in the latter case the leucocyte may have enclosed the parasite.

As has already been stated, in the fresh blood removed from the body and examined for a while under the microscope the polymorphonuclear leucocytes can be seen to engulf pigment and certain parasitic forms—viz. extracorpuscular forms, especially degenerated and fragmented forms, segmenting forms and spores, and altered red corpuscles—and especially do they attack the flagellate bodies, as has been demonstrated by Thayer and Hewetson (Plate II. Figs. 45–49). Such enclosed parasitic forms, with the exception of the spores, can be seen rapidly to become indistinct and unrecognizable within the leucocytes.

From the examination of the fresh circulating blood alone one obtains a very inadequate conception of the extent and nature of the phagocytic processes in malaria. A fuller idea of these processes can be derived from the study of blood withdrawn by puncture of the spleen, where phagocytic phenomena are far more active than in the circulating blood; but it is especially in the microscopical examination of the organs of those who have succumbed to a malarial attack that the best opportunity is afforded to learn the extent of phagocytosis in malaria. Here one finds abundantly leucocytes, endothelial cells, and macrophages containing pigment, parasitic forms, and altered red blood-corpuscles.

Parasites in their later stages of development, especially when they are free, are frequently taken up by phagocytes—in their early stages rarely, unless they have become extracorpuscular or the corpuscle containing them is degenerated. Sporulating forms, and somewhat less frequently forms with collected pigment (presegmenting bodies), are the ones most commonly found in a recognizable condition within the phagocytes. It is stated by Bastianelli and Bignami that the bodies with pigment blocks (presegmenting) are found most frequently within macrophages, and sporulating forms within polymorphonuclear leucocytes. Pigmented amœbæ they found rarely, and red blood-corpuscles containing unpigmented amœbæ very rarely, within phagocytes. Bastianelli gives the following as the order of frequency in which the various parasitic elements are found within phagocytes: (1) pigment; (2) sporulating forms and spores; (3) red corpuscles, normal or decolorized, containing sporulating forms or bodies with central pigment blocks; (4) brassy and decolorized red corpuscles containing plasmodia (hyaline bodies in the amœboid stage); (5) free bodies with central pigment clumps; (6) more rarely free amœbæ or red corpuscles of normal appearance containing parasites in the amœboid stage. According to the observations of the writer, free bodies with central pigment clumps occupy a higher place in this scale than that assigned to them by Bastianelli. Crescents enclosed in phagocytes may be found even in the circulating blood. The various bodies within phagocytes often lie in an area surrounded by a clear zone like a vacuole.

Golgi (1887–88) discovered that phagocytosis occurs in quartan and tertian infections with a definite periodicity which stands in relation to certain phases in the cyclical development of the parasite, and therefore to certain periods of malarial fever. This is readily understood when one considers that it is especially the free pigment and the mature and segmenting parasites and the degenerative forms which are taken up by phagocytes. The pigment is liberated by the process of sporulation which, as has already been explained, occurs shortly before and during the early stages of the paroxysm. Corresponding with this, Golgi found that pigmented leucocytes are present in the circulation during the paroxysm and for a short time afterward, and that they disappear from the circulation during the apyrexia. This periodicity in the appearance of melaniferous leucocytes and of other phagocytes can be observed regularly in quartan and tertian infections. There are frequently indications of it also in æstivo-autumnal infections, but on account of the irregularities in the cyclical development of the Hæmatozoön falciparum, of the prolonged period of sporulation, of the frequent occurrence of multiple groups of parasites, and of the presence at all periods of degenerated red corpuscles, this periodicity in the occurrence of phagocytosis is often obscured or is not manifest at all. Pigmented leucocytes may be found in many cases of æstivo-autumnal infection during all periods of the disease, although they are more numerous during the paroxysm and shortly afterward. In the severe prolonged cases they are generally abundant, and they may persist in the circulation for several days after cure is effected. As long as crescents are present pigmented leucocytes may be found.

Parasites which, to all appearances, are normal are found within phagocytic cells. What is the fate of such enclosed parasites? That many degenerate and die cannot be questioned, for these degenerative alterations can be directly observed in progress under the microscope in examining fresh blood, and in studying malarial blood and tissues one frequently encounters evidences of this fate of the parasites. It is claimed, however, by Marchiafava, Bignami and Bastianelli that enclosed spores, although prevented from further development, may survive for a long time within leucocytes and other cells, and that such latent spores may after an indefinite period be set free and cause by their development a relapse of the fever.

Attention has already been called to Golgi's belief that the æstivo-autumnal parasite may, and to a considerable extent does, develop within the leucocytes and endothelial cells of internal organs, in ordinary cases chiefly of the spleen and bone marrow. He adduces a number of considerations in support of this view, but the objective evidence he and his pupil, A. Monti, find in the detection of the frequent presence of this parasite, apparently intact and in all stages of development, within these cells. In opposition to Golgi, however, it is claimed by Marchiafava, Bignami and Bastianelli that early phases of development of the parasite are rarely seen within the cells, and that, therefore, the much more commonly enclosed late phases cannot have developed within the cells from young parasites. Golgi also brings to his support the observation, made by all who have studied the subject, that many of the cells containing parasites degenerate and die, as is made evident especially by the loss of their nuclei. He interprets this as meaning that in the conflict between cell and parasite the latter often comes off the victor. Further investigations are needed to determine to what extent Golgi's doctrine as to the intercellular residence and development of the Hæmatozoön falciparum is correct. Certainly the greatly preponderating number of intact æstivo-autumnal parasites observed in examining the organs of those dead of pernicious malaria are found within free red blood-corpuscles in the vessels of internal organs.

The theory of Metchnikoff that the essential factor in the resistance of the body to the malarial parasite resides in the activities of phagocytes is opposed by many considerations. The most important factors in determining the gravity and the course of a malarial infection are the degree and quality of virulence possessed by the parasite, on the one hand, and the resistance of the individual receiving the parasite, on the other hand. There is no evidence that phagocytic functions are in abeyance in severe and pernicious cases of malaria. On the contrary, we find here often enormous numbers of parasitic enclosures within phagocytes. There is no proof that spontaneous recoveries from malaria are associated with an increase of phagocytic activity. Inasmuch as phagocytes regularly attack degenerated and fragmented parasites, and as we know that such degenerations occur frequently within parasites free in the plasma, it is permissible to suppose that many of the parasitic forms found within phagocytes were already impaired in their vitality before they were engulfed by cells. After the administration of quinine, which directly injures the malarial parasite, a distinct increase in the number of phagocytes has been often observed. Certainly quinine does not stimulate the leucocytes to swallow the parasites. Here the increase in the phagocytes must be attributed to the increase in the number of damaged parasites.

There is evidence that the blood-plasma may exert a parasiticidal effect upon the malarial organism, as well as upon other protozoa (Faggioli), when the parasite has escaped from the protective covering of the red blood-corpuscle. The period when the largest number of malarial parasites are destroyed is that of sporulation and of free spores, and it is during this phase of the life-history of the parasite that quinine acts most effectively. We may, at least provisionally, adopt a theory to explain natural resistance to the malarial parasite similar to that which many accept regarding resistance to bacteria—viz. that the parasites are destroyed by parasiticidal substances contained both in the plasma and within leucocytes and other phagocytic cells. The substances injurious to the parasite are in the last analysis furnished to the plasma by the cells, and are in a more concentrated or potent form within the cells than in the fluids. This theory assigns to the phagocytes a higher rôle than that of mere scavengers. They are endowed in especial degree with the power of destroying the parasite, but this power is shared by the plasma.

PATHOGENESIS.

The discovery of the malarial parasite has placed within our reach the means of solving many problems concerning malaria which we could not formerly even attack with any hope of success. Already we have attained a satisfactory understanding of not a few previously unexplained manifestations of malaria, and other formerly obscure malarial phenomena have been brought at least within the range of our comprehension. Much still remains to be elucidated, but we cannot doubt that further studies will continue to throw fresh light upon what remains obscure.

In the description of the symptoms and lesions of malaria attention will frequently be called to their relations to the parasite, and in this connection only certain salient points, relating more particularly to pathogenic properties of the parasite, require consideration.

The mere presence of the malarial parasite in the body is not sufficient to cause symptoms. The organisms must have multiplied to a certain point before their presence is manifested by recognizable symptoms. The bearing of this fact upon certain malarial phenomena, more particularly upon the varying periods of incubation as determined by experimental inoculations of malarial blood and upon fevers with long intervals, will be considered in the clinical part of this article.

It may be stated as a general rule, which was first formulated by Golgi, that the larger the number of organisms present in the body the more severe are the manifestations of the disease; but the number of the organisms is by no means the only factor which determines the gravity of the disease. The variety of parasite which is concerned in the infection is a factor of fundamental importance. The quartan variety produces the mildest attacks, the tertian is more virulent than the quartan, and the æstivo-autumnal variety is the most virulent of all, and is the one which is almost exclusively associated with the pernicious attacks. These variations in virulence are best explained upon the assumption that the malarial organism produces toxic substances of varying virulence according to the variety of parasite. There is also clinical evidence that one and the same variety may vary in virulence, so that, for example, some æstivo-autumnal parasites are more virulent than others.

In seeking an explanation of the varying clinical characters of malarial infections we have to reckon not only with the number, the varieties, and the virulence of the parasites, but also with several other factors, such as predisposing conditions on the part of the individual infected, the occurrence of multiple groups of the parasite, the distribution of the organisms in internal parts, the circulatory and other anatomical disturbances induced by the parasites.

Periodicity is the most striking clinical characteristic of malarial fevers, and the explanation of this phenomenon has exercised the minds of pyretologists from ancient times. It is true that intermittence is not limited to fevers of malarial origin, but regularity of rhythm in the occurrence of the paroxysms is especially characteristic of malaria. One of the most interesting additions to our knowledge resulting from the discovery of the malarial parasite is the demonstration by Golgi, which has been abundantly confirmed, that this rhythm in the malarial paroxysms corresponds to a rhythm in the development of successive generations of the parasite.

The onset of each paroxysm corresponds to the ripening and sporulation of a generation of parasites and the setting free of a new brood.[1]

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[1] The old idea that the periodicity of malarial fevers depends upon the periodical production in the blood of a *materia peccans* is thus confirmed. It is interesting in this connection to note the line of argument presented by Griesinger in his admirable and sug-

Exactly what the connection is between this act of sporulation, with the liberation of a fresh brood of young parasites, and the cause of the febrile paroxysm, is not definitely known. It was at first suggested by Golgi (1887) that the paroxysm is due to the invasion of the red blood-corpuscles by the new group of parasites, but it was shown by Antolisei (1890) that the paroxysm depends rather upon the act of segmentation than upon the invasion of the blood-corpuscles by a new generation of organisms, for quinine, administered before a paroxysm in sufficient quantity, may, by destroying the fresh brood, completely prevent the invasion of the red corpuscles, but it cannot prevent the segmentation and the impending paroxysm. The view is now widely held, and seems plausible, that in the act of sporulation and of liberation of the spores chemical poisons are set free, and that these poisons, by their action on the nervous centres concerned in the production of fever, cause the febrile paroxysms. This toxic theory of malaria has been elaborated especially by Baccelli.

The fact that the malarial parasite resides in, feeds upon, and destroys the red blood-corpuscles furnishes an entirely satisfactory explanation of two of the most characteristic and important manifestations of malaria—the melanæmia and the anæmia. The malarial pigment, for which we formerly had no adequate explanation, is formed as an undigested residue within the body of the parasite by metabolic processes directly out of the hæmoglobin of the infected red blood-corpuscle. Various stages of the formation of the pigment within the parasite can be seen. The liberation of this pigment, its inclusion by phagocytes, its deposition in various internal organs, have all been described, and will be further considered under the *Pathological Anatomy.* The relations of the biological characters of the parasite to malarial anæmias and to hæmoglobinuria will be fully considered in the anatomical and clinical parts of this article (pages 93, 116, 125, and 130).

The ways in which the red blood-corpuscles may be altered by the action of the malarial parasite are various. The extent of these changes varies with the variety and the virulence of the parasite. They are least in quartan infections, greatest in the æstivo-autumnal. The infected blood-corpuscle may appear otherwise normal. It may be swollen or shrunken or variously deformed. It may divide into two or more pieces. It may be partly or completely decolorized, or the hæmoglobin may separate from the stroma and be dissolved in the plasma, or may be concentrated around the parasite. Especial significance in the æstivo-autumnal infections attaches to that alteration in the cor-

gestive article on the malarial diseases (*Virchow's Handb. d. spec. Path. u. Therap.*, Bd. ii. Abth. 2, 2te Auflage, p. 41, Erlangen, 1864): "The cause of the periodicity of the fever cannot, therefore, be referred to the disposition of the nervous system to rhythmical vital actions, as many have formerly done, but it must, at least according to our present although very incomplete knowledge concerning the causes of heat, be attributed to something periodically occurring in the blood, which is connected with the increased production of heat. It has been formerly conceived that a certain substance, a *materia peccans*, appears periodically in the blood and incites the febrile heat and reaction: this material requires for its production and complete development sometimes longer, sometimes shorter, periods, and herein lies the cause of the rhythm of the fever. . . . . As an explanatory hypothesis this conception accomplishes more than the later attempts at explanation. . . . The continuous morbid process which causes the poisoning incites periodically changes in nutrition or in the blood which arouse the nervous apparatus to abnormal manifestations."

puscle which has been repeatedly referred to as the brassy change, on account of the resemblance in the color of the shrunken corpuscles to brass, sometimes compared also to copper or old gold. Nor are the corpuscles which are actually infected by the parasite the only ones which may be altered. Uninfected corpuscles may also be changed in appearance, and may be destroyed, especially in cases of hæmoglobinuria.

These changes in the red blood-corpuscles, which must be regarded as degenerative and destructive, cannot be brought wholly into parallelism with the development of the malarial pigment. In fact, the most profound lesions and the greatest destruction of the red corpuscles occur in infections with the æstivo-autumnal parasite, which is characterized by the small amount or even the entire absence of pigment. To explain many of these changes we must have recourse again to the theory that toxic substances are produced by the parasite and directly damage the blood-corpuscles.

These alterations in the red blood-corpuscles not only explain the malarial anæmias and the hæmoglobinuria with their concomitant symptoms and lesions, and the accumulation of malarial and other pigments in certain organs, but they are utilized, although less conclusively, to explain certain other malarial phenomena. We know from physiological observations that the physical integrity of the red blood-corpuscles is an important condition in the maintenance of their circulation within the blood current. It is reasonable to suppose that corpuscles as profoundly altered as are many of those infected with the malarial parasite will circulate with difficulty, and will tend to accumulate in certain situations where local conditions of the circulation favor the lodgement of foreign particles which get into the circulation. Many writers, therefore, attribute to these alterations in the physical properties of the infected red corpuscles the accumulation of the parasites within the vessels of certain internal organs, more particularly the spleen, the bone marrow, the liver, and the brain, and they explain the absence of such accumulation in quartan infections by the comparatively slight lesions of the infected corpuscles, and the large accumulation in tertian, and still more in æstivo-autumnal, infections by the more serious damage inflicted upon the infected red corpuscles by the varieties of the parasite causing these latter infections. Doubtless these factors—changes in the infected red corpuscles and local conditions of the circulation—are important in determining the localization of the parasites in certain internal parts, but with our present knowledge we cannot explain the varying distribution of the parasites observed in different cases exclusively by their aid, any more than we can adopt a similar explanation for the localization of the micro-organisms in other infections.

The localization of the parasites in some cases, more particularly in æstivo-autumnal infections, within definite vascular areas of internal organs stands in relation to corresponding symptoms and lesions. The comatose and the choleriform types of pernicious malaria are associated with an accumulation, which may be enormous, of the parasites in the capillaries and small vessels of the brain and of the stomach and intestine respectively. Other special localizations of the parasites will be mentioned in the subsequent part of this article. In these cases cap-knowledge, better explained by the toxic theory of the pathogenic action of the malarial parasite than by any mechanical theories which have yet been offered.

We have, however, no positive demonstration of the existence of specific malarial toxins. The investigations as to the toxicity of the urine of malarial patients will be described on page 123. They have not led to any positive results as to the detection of specific malarial poisons.

It is a very old conception that the febrile reaction of the malarial paroxysm is conservative in the sense that this response of the body to the presence of pyogenic agents in some way aids in the elimination or destruction of injurious substances. This conception is not altogether without support from the parasitological study of malaria. The fever begins at the time of the birth of a new generation of parasites. These young organisms before they have entered the red blood-corpuscles are, of all phases of development of the parasite, in the most vulnerable condition, as has been shown by investigations of the action of quinine. That a large number of them perish during the febrile paroxysm seems to be demonstrated, at least in quartan and tertian infections, by the contrast between the number of sporulating forms and the number of succeeding infected corpuscles. Especially suggestive of increased potency of parasiticidal agencies during the febrile paroxysm are cases, especially of quartan or tertian infection, in which, after a sharp paroxysm, the symptoms and the parasites disappear, perhaps permanently, but often to return after a long interval as a recrudescence of the fever (page 121).

SIMILAR HÆMATOZOA IN THE LOWER ANIMALS.

Great interest attaches to the presence in the blood of certain lower animals of protozoan parasites closely resembling the malarial parasite. Attention was first called to this resemblance by Danilewsky (1885–86), who described more fully certain forms which were previously known, and added the discovery of new forms, especially that of hæmatozoa in birds which bear close resemblance to the human malarial parasite. Since Danilewsky's first publications there have been a number of investigations on this subject by Kruse, Celli and Sanfelice, Grassi and Feletti, Laveran, Labbé, and others.

In the blood of frogs, turtles, lizards, and some other cold-blooded animals hæmatozoa presenting some points of resemblance to the malarial parasite are not uncommon. Of these the best studied and most interesting is the DREPANIDIUM RANARUM (Lankester), identical with Gaule's "Würmchen," in the blood of frogs. It is, however, certain hæmatozoa in birds which bear such close resemblance to the malarial parasite that their identity with the latter has been assumed by Danilewsky and Grassi and Feletti, who speak of the existence of malaria and of malarial parasites in these animals. Most of the observations thus far reported have come from Russia and Italy, but the parasites have been found in birds also in Germany and France, and recently in the United States.

In birds thus infected have been found forms similar to those of the malarial parasite in man—viz. unpigmented and pigmented hyaline bodies (which, however, in distinction from similar bodies in man, manifest little or no amœboid movement), sporulating forms, crescents, and flagellated bodies. The bird's hæmatozoa are also parasites of the red blood-corpuscles, from which they produce black pigment: they pass through the same stages of development as the latter, and the same diversity of views exists as to the origin and significance of the crescents and flagellated bodies. The name HÆMOPROTEUS was introduced by Kruse to designate these so-called malarial parasites of birds, and various other names have also been suggested. Grassi and Feletti adopt the same names and the same classification for these parasite of birds as for the human parasites (page 38). There are differences between the hæmatozoa found in different species of birds, and in the same species apparently different varieties of the parasite have been observed, but there are at present no definite classification and no certainty as to the number of varieties which may exist.

Although these hæmatozoa of birds evidently belong to the same class of organisms as the malarial parasite, there are several reasons which indicate that they are not identical with the latter. They present certain morphological and physiological differences which it would lead too far here to describe. Although found thus far chiefly in birds from malarial regions, it is not proven that they may not exist in birds elsewhere. The inoculation of uninfected birds with the blood of birds containing the parasites has been, in a large preponderance of the experiments, unsuccessful in the result. The inoculation of birds with blood from human beings affected with malaria, and the inoculation of human beings with the blood of birds containing the hæmatozoa, have been uniformly without positive result (Di Mattei). Large doses of quinine have no influence upon the parasites in birds. The presence of the hæmatozoa in birds is usually without recognizable disturbance of the health of the birds, although it may cause a chronic or an acute affection. While, then, we must admit a close relationship between certain hæmatozoa of birds and the human malarial parasite, the existing evidence is opposed to their identification.

DESCRIPTION OF PLATES I. AND II.[1]

The drawings were made with great care and skill by Mr. Max Broedel, with the assistance of the camera lucida, from specimens of fresh blood. A Winkel microscope, objective, 1-14 (oil-immersion), ocular, 4, was used.

Figs. 4, 13, 23, 24, and 42 of Plate I. were drawn from fresh blood, without the camera lucida.

PLATE I.

The Parasite of Tertian Fever.

1.—Normal red corpuscle.

2, 3, 4.—Young hyaline forms. In 4 a corpuscle contains three distinct parasites.

5, 21.—Beginning of pigmentation. The parasite was observed to form a true ring by the confluence of two pseudopodia. During observation the body burst from the corpuscle, which became decolorized and disappeared from view. The parasite became, almost immediately, deformed and motionless, as shown in Fig. 21.

6, 7, 8.—Partly developed pigmented forms.

9.—Full-grown body.

10–14.—Segmenting bodies.

15.—Degenerative form simulating a segmenting body.

16, 17.—Precocious segmentation.

18, 19, 20.—Large swollen and fragmenting extracellular bodies.

22.—Flagellate body.

23, 24.—Degenerative forms showing vacuolation.

The Parasite of Quartan Fever.[2]

25.—Normal red corpuscle.

26.—Young hyaline form.

27–34.—Gradual development of the intracorpuscular bodies.

35.—Full-grown body. The substance of the red corpuscle is not visible in the fresh specimen.

36–39.—Segmenting bodies.

40.—Large swollen extracellular form.

41.—Flagellate body.

42.—Degenerative form showing vacuolation.

PLATE II.

The Parasite of Æstivo-autumnal Fever (*Hæmatozoön falciparum*).

1, 2.—Small refractive ring-like bodies.

3–6.—Larger disk-like and amœboid forms.

7.—Ring-like body with a few pigment granules in a brassy, shrunken corpuscle.

8, 9, 10, 12.—Similar pigmented bodies.

11.—Amœboid body with pigment.

13.—Body with a central clump of pigment in a corpuscle showing a retraction of the hæmoglobin-containing substance about the parasite.

14–20.—Bodies with central pigment clumps or blocks. Presegmenting forms.

21–24.—Larger bodies with central pigment blocks. Presegmenting bodies. Seen in the peripheral circulation during a severe paroxysm.

25–28.—Segmenting bodies from the spleen. Figs. 25–27 represent one body where the entire process of segmentation was observed. The segments, eighteen in number, were accurately counted before separation, as in Fig. 27. The sudden separation of the segments, occurring as though some retaining membrane were ruptured, was observed.

29–37.—Crescents and ovoid bodies. Figs. 34 and 35 represent one body which was seen to extrude slowly, and later to withdraw, two rounded protrusions.

38, 39.—Round bodies.

40.—Pseudo-gemmation, fragmentation.

41.—Vacuolation of a crescent.

42–44.—Flagellation. The figures represent one organism. The blood was taken from the ear at 4.15 P. M.; at 4.17 the body was as represented in Fig. 42. At 4.27 the flagella appeared; at 4.33 two of the flagella had already broken away from the mother body.

45–49.—Phagocytosis. Traced with the camera lucida.

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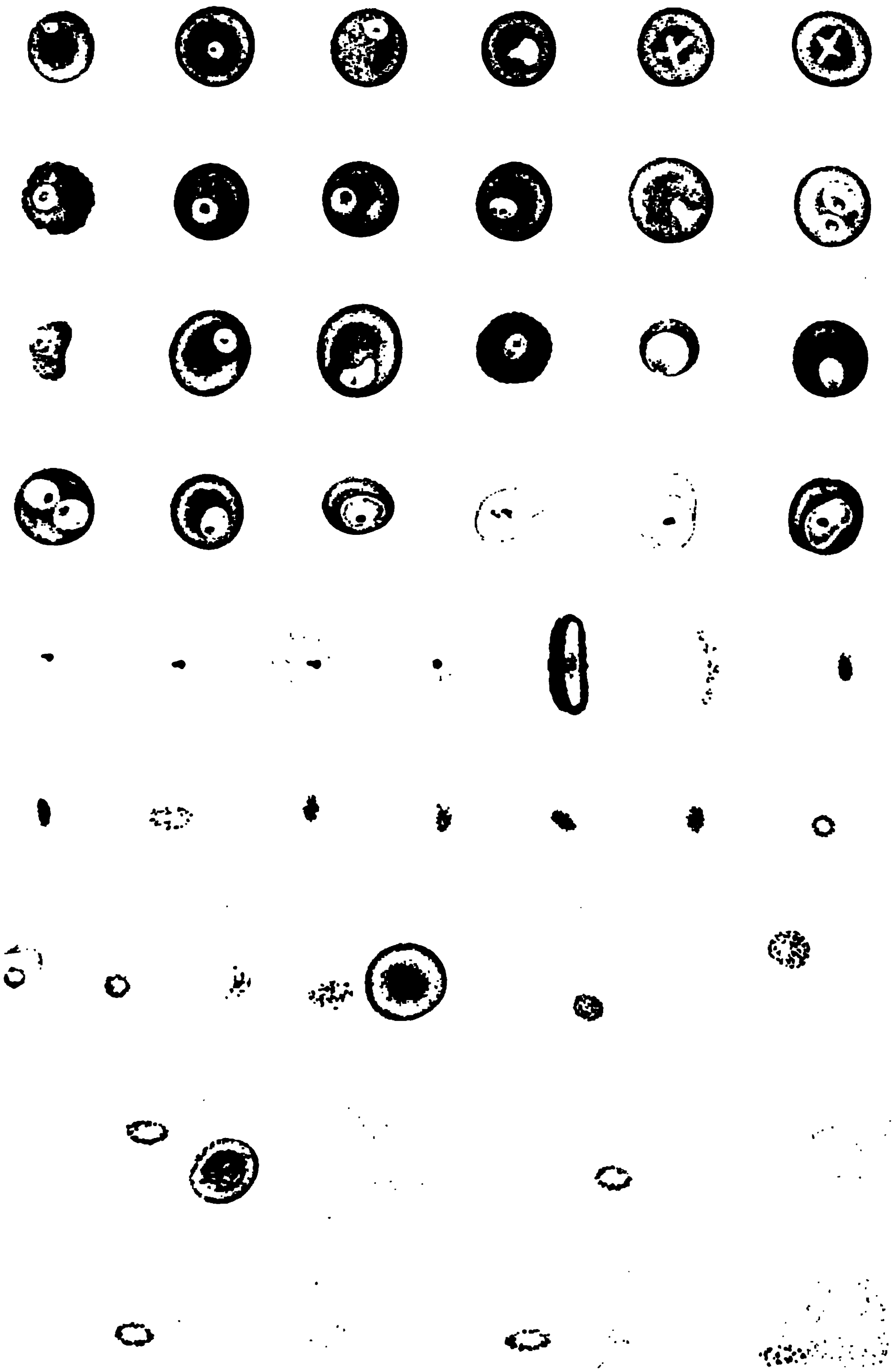
[1] These plates are taken by permission from *The Johns Hopkins Hospital Reports*, vol. v., 1895. Four figures—viz. Figs. 21, 22, 23, and 24—have been added to Plate II., and are also from the drawings of Mr. Max Broedel.

[2] The color of the pigment in these figures of the quartan parasite has too much of a reddish tint.

PLATE II.

[illegible]



ETIOLOGY, PATHOLOGICAL ANATOMY, SYMPTOMS, DIAGNOSIS, PROGNOSIS, AND TREATMENT.

BY WILLIAM S. THAYER, M. D.

ETIOLOGY.

DISTRIBUTION.—The malarial fevers are widely distributed, occurring in almost all regions of the earth. There are, however, certain principal foci where the disease is permanently endemic. These regions are chiefly in the warmer temperate and tropical countries. Generally speaking, the farther one departs from the equator the less common are the malarial fevers. A sharp line of delimitation cannot, however, be drawn. Occasionl cases have, according to Celli,[1] been observed as far north as Irkutsk in Siberia, Haparanda in the Gulf of Bothnia (65° N. latitude), Juliushaab, Southern Greenland, and New Archangel in Alaska, while to the south malaria has been reported to exist as far as the isotherm of 60°. It must, however, be remembered in considering any statistics concerning the distribution of malaria that the diagnosis of malarial fever has been, until very recently—and is, alas! far too frequently today—made upon a very insufficient basis. In many regions today an intermittent fever with chills is without further investigation assumed to be of malarial origin, and even at the present time, in some of the large cities of this country, there are official statistics of mortality due to malaria—statistics showing thousands of deaths every year—which are almost absolutely incorrect.

About the main foyers of malaria there is, however, little doubt. In Europe the disease is common in the low lands about the coasts of Italy, Sicily, Corsica, Greece, the Black and Caspian Seas, and in the lands bordering upon the Po, the Tiber, the Danube, and the Volga. About the coast of certain parts of France, Spain, and in Denmark and Sweden, an occasional case is seen. In Holland and Belgium the milder forms of the disease are not uncommon, while a few cases of the same nature are seen in Germany about the mouth of the Elbe and along the Baltic coast of Prussia, in Silesia, the plain of the river Mark, and in Pomerania. In tropical Africa the disease appears in its most severe forms, especially along the West Coast. The chief foyers of the disease in Europe are in Italy and Southern Russia. In India, Ceylon, and in the East Indies it is particularly common, while in Southern and Southwestern China it is also endemic. In Japan the disease is rare. In the Western Hemisphere malaria is seen in the lowlands about the coast from New England to Florida, though above Virginia the severe forms are rare. In the Gulf States and along the banks of the Mississippi and its tributaries, in most of the Southern States, the disease is almost always present. About some of the Great Lakes, both in the United States and Canada, malarial fevers are occasionally seen, while a certain number of cases are reported from the Pacific coast.

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[1] *Verhandl. d. X. Internat. Med. Cong.*, Bd. v. Abth. xv. p. 68.

In Cuba, Mexico, and Central America some of the most fatal forms of the disease are met with. The much feared Chagres fever of the Isthmus of Panama is a pernicious malarial infection. About the lowlands of the eastern coast of South America, particularly in the Guianas and in Brazil, the disease is endemic in its most malignant forms. On the west coast it is less frequent, though its occurrence in Peru and Bolivia has been known for years. Indeed, it is from the Peruvian Indians that we learned the value of the specific remedy for the disease. In Australia, New Caledonia, and the islands of the Pacific the disease is very rare, and in some regions, such as Hawaii, Samoa, New Zealand, and Van Diemen's Land, notwithstanding the existence of extensive low marshy tracts, it is quite unknown.

In cases of malarial fever which occur sporadically in regions where the disease is uncommon the infection may often be traced to a previous sojourn in a malarious district. Extensive epidemics and pandemics of malarial fever, spreading over the greater part of the earth, have been described. In most of these instances, however, considerable uncertainty exists as to the true nature of the process.

PHYSICAL GEOGRAPHY.—The physical geography of the country has much to do with the prevalence of malarial fever. In the words of Laveran, "The principal foyers of paludism are situated on the coast or along the banks of large rivers." High altitudes are usually free from malarial fever, and the mountains and plateaus in the neighborhood of malarial districts are often used as sanitaria by the inhabitants. The high altitudes may not, however, be a protection, as, according to Hertz,[1] fevers occur in the Tuscan Apennines at a height of 1100 feet, in the Pyrenees at 5000 feet, on the island of Ceylon at 6500 feet, in Peru at from 10,000 to 11,000 feet. It is, however, by no means improbable that many of these fevers which have been called "malarial" are, in reality, of some other nature. This has been shown to be true in the case of the "mountain fever" of the Western States, which is for the most part, probably, typhoid fever.

THE SOIL.—Low, marshy regions are particularly likely to be malarious; hence the term "paludism" which is so generally used. Mixed salt and fresh water marshes seem to be particularly favorable for the development of the disease. Low, moist, ill drained lands, rich in vegetable matters—lands which have been allowed to fall out of cultivation—are particularly dangerous. All marshy regions, however, even in tropical countries, are not of necessity malarious, an example of this being shown in some of the South Pacific islands, as already mentioned. And, while the disease is particularly common in marshy districts, it may occur in other regions in sandy or clayey soil, or, indeed, in rocky regions. An impervious subsoil is believed to be particularly dangerous.

Effects of Turning up the Soil.—In many instances the denudation of a soil covered by forests or rank vegetation, or the turning up of the soil in a district which was previously free from the disease, may be followed by an outbreak of malarial fever, while in other regions where the disease already exists similar interference with the vegetation or the soil may greatly intensify the severity of the process. An example of this latter condition is shown in the severe outbreak of malarial fever which was associated with the excavation of the Panama Canal. In Paris, which for many years had been free from paludism, the digging of the Canal Saint Martin, and again, in 1840, the excavations for the fortifications, were, in each instance, followed by an outbreak of characteristic intermittent fever. Irrigation of low lying districts without proper drainage has been followed by an outbreak of malaria or an increase in the severity of the cases. Such a condition of things has been noted in some of the irrigated districts in Southern California.

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[1] *v. Ziemssen's Cyclopædia of the Practice of Medicine,* vol. ii.

Effects of Drainage.—Efficient drainage of marshy districts which have been rich in malarial fevers has a marked effect upon the frequency and severity of the manifestations of the disease. Years ago malaria was common in the surroundings of London, which were marshy and ill-drained; today, thanks to good drainage, the disease is unknown. The low lands of Holland used to be the seat of very severe malaria; today, only occasional cases of the mildest forms of the disease occur. The effect of good drainage upon the Roman Campagna has been very striking, the severity of malarial fever diminishing materially.

Cultivation.—The cultivation of many marshy, malarious districts has been followed by a marked improvement in the sanitary condition. The planting of trees has been supposed to have a particularly good effect, possibly because of the drainage of the soil which is thus accomplished. For some time it was supposed that certain trees, particularly the *eucalyptus globulus*, had an almost specific effect in protecting the neighborhood against malarial fever. The advantages of this particular tree have, however, been much exaggerated. Malarial fever never originates at sea. Those cases which have been reported date their infection, unquestionably, to some period before the voyage. There is much to suggest that the soil has some intimate connection with the development of the contagium of paludism.

VARIATIONS IN DISTRIBUTION.—One of the most striking characteristics of malarial fever is the manner in which it leaves one region in which it has existed for some time, to appear in another which may, for a considerable period, have been quite free from any manifestations of the disease. This change in the distribution of the disease is in great part due to the activity of man. On the one hand, an outbreak may follow the abandonment or neglect of richly cultivated areas which have been well drained and taken care of, as, for instance, the Roman Campagna in the time of Augustus, while, again, in other regions the turning up of the soil may bring about an outbreak where it is least expected. But this explanation does not answer all cases. The appearance of malarial fevers in the New England States during the past fifteen years, after a long period of almost entire quiescence, is a striking example of these inexplicable changes in location. Again, in districts where malaria is permanently endemic there are often cycles in the severity of the disease which are impossible to explain.

CLIMATE.—Heat and moisture are important for the development of the fever. In malarious districts a very dry season is usually more healthy. Laveran[1] states that in Algeria the rainy years show a more severe endemic than the dry, while the first "rains of the autumn give rise, almost always, in Algeria to a recrudescence of the fever."

SEASON.—In tropical countries malaria exists usually throughout the year, but it is almost always most severe in the summer and fall. As one approaches the temperate climate the cases in winter and spring become very rare. Along the eastern coast of the United States, just as in Rome, the cases in the winter are very few, while with the spring a certain number of infections begin to appear. It is, however, not until July that the real malarial season begins. The height of the malarial season is reached in the months of August, September, and October. The following table, showing the number of cases of malarial fever treated at the Johns Hopkins Hospital between January 1, 1890, and January 1, 1894, gives a good idea of the variations in the occurrence of the disease to the seasons of the year:

Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Total.
9	8	8	17	21	18	38	66	122	120	38	25	490

The earliest cases show also the mildest types of infection. Thus, in the spring the first cases are usually tertian or quartan infections. As the season advances double tertian infections become more frequent, while at the height of the malarial season the majority of cases are of the æstivo-autumnal type, the most severe form of malaria. Thus, out of 542 cases analyzed by Hewetson and the author,[2] there were—

	First half year.	Second half year.
Regularly intermittent fevers	113	230
Æstivo-autumnal fevers	5	183
Combined infections	3	8
	121	421 = 542

At the height of the malarial season, during the months of September and October, there were—

Regularly intermittent fevers	109
Æstivo-autumnal fevers	120
Combined infections	5

This observation concerning the variation of the types of the fever with the times of the year is as old as Hippocrates. It has long been popularly supposed that the early cases of fever in the winter and in the spring represent, *in toto*, relapses from infections of the preceding fall, the fevers of first invasion beginning only with the summer months. The analyses of our cases at the Johns Hopkins Hospital tend, however, to show that, while the proportion of fevers of first invasion is less in the spring than in the summer months, yet they do occur.

WINDS.—There is much which tends to suggest that the infective agent may be carried by the wind. It has been asserted, for instance, that along the banks of a stream in a malarious district the fevers are often more frequent and severe on the side toward which the prevailing winds blow. Again, in other instances it has appeared that strips of forest land have arrested the spread of the disease, suggesting that some infectious substance may be filtered out by the trees. Thus, Lancisi believed that it was through the influence of the winds that the Roman Campagna became more unhealthy after the removal of the sacred groves. These, he believed, acted as a protection by filtering from the air infectious substances carried by the winds which blew over the Pontine marshes.

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[1] *Traité des Fièvres palustres*, Paris, 1884, p. 8.

[2] "The Malarial Fevers of Baltimore," *Johns Hopkins Hospital Reports*, vol. v.

ALTITUDE.—It has been repeatedly observed that in malarious districts the dangers of infection are much greater close to the ground. Sleeping upon the ground is particularly dangerous. The upper stories of a house are safer than the lower. Infection appears to take place more readily by night than by day.

DRINKING WATER.—Many have laid, and still do lay, much stress upon drinking water as the source of the disease. The experiments, however, of Celli,[1] Marino,[2] and Zeri,[3] who caused individuals to drink in large quantities water which was obtained from the most malarious districts, without any bad effects, and of Grassi and Feletti,[4] who fed individuals upon dew collected from malarious regions, with similar negative results, are strong arguments against this idea. It should be remembered, however, that while these experiments are strong evidence that the malarial poison is not introduced through the drinking water, yet it is no proof that water may not contain the parasite, or, indeed, form an actual culture medium for some forms of the organism. We are wholly ignorant of the manner of entry of the parasite into the system, of the form in which it exists outside of the body, or of the changes which it may pursue in other media than the circulating blood. It is not impossible to imagine a body which might pursue a part of its development in water, reaching its truly infectious form only in a later stage and in some other medium.

Grassi and Feletti have shown that the living parasite from the circulating blood does not, when ingested, cause fever. Thus, they caused an individual to drink the fresh blood of a malarial patient without result, while inoculation experiments with similar blood are almost always positive. (See page 34.)

RACE.—In many malarial districts the natives—negroes, Arabs, Indians, Tamils—appear to have a relative insusceptibility to the disease, the degree of which varies in different localities and according to different authors. Our observations in Baltimore would tend to show that here the susceptibility of the negro is only about one third that of the white.

OCCUPATION.—The occupation has much to do with susceptibility to the disease. Soldiers and tramps who sleep upon the ground in malarious districts are particularly susceptible. Fishermen in the bays and inlets along the southern coast of the United States, as well as farmers and berry pickers in the same regions, are particularly open to infection.

AGE has apparently no effect upon the susceptibility, excepting in so far as the very young and the very old are less likely to be exposed.

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[1] *Bull. d. Soc. Lanc. d. Roma*, 1886, vi. 1, 39 (5 Dec., 1885).

[2] *Riforma Medica*, 31 Oct., 1890, No. 251, 1502.

[3] *Bull. d. R. Acc. Med. di Roma*, 1889–90, xvi. 244.

[4] *Centralblatt für Backt.*, 1891, ix. 403, 429, 461.

Predisposing Causes.—It is generally believed that in malarious districts almost anything which tends to diminish the vitality of the patient acts as a predisposing cause to malarial infection. It is often asserted that where a previous attack has existed injuries of various sorts are particularly likely to be followed by a relapse of the malaria. It has been asserted, for instance, that an injury to the spleen in a patient who has formerly had malarial fever may call forth a relapse. With regard to the effects of traumatism, the observation of nearly a thousand cases during the last five or six years has not given any positive answer, while the complications of malaria with other acute diseases have been, perhaps, rather surprisingly infrequent. It seems reasonable that trauma or operation, by reducing the condition of the patient, should render him more susceptible to a fresh malarial infection or more liable to a recrudescence of an already existing process. The fact, however, that in nearly seven years not a single case of post-operative malaria has occurred in the Johns Hopkins Hospital has led us to believe that many of the chills occurring under these circumstances, generally supposed to be malarial, are probably, in reality, septic in origin.

Manner of Infection.—The discoveries of Laveran have revealed to us the infectious agent in malaria, while its specific action has been abundantly demonstrated by clinical observation and inoculation experiments. And yet it must be confessed that we are wholly ignorant as to the manner in which the parasite exists outside of the body or how infection takes place. The most important points of entry into the system which have been suggested are—

(1) The respiratory tract;
(2) The digestive tract;
(3) The skin (insect bites, etc.).

(1) There is a very general belief that infection may take place through the respiratory tract, though positive proof of its occurrence is as yet wanting. In favor of this view are the observations of Lancisi and others concerning the winds.

(2) Many observers, as has been said, still believe that the parasite is introduced chiefly through the digestive tract. The observations, however, of Celli, Marino, Żeri, Grassi and Feletti, already referred to, are very suggestive evidence against this idea.

(3) The inoculation experiments referred to in the description of the parasites have given positive proof that infection may take place when the parasite is introduced beneath the skin. This renders more plausible the old idea that insect bites may sometimes serve to convey the contagium. In this connection one may remember the remarkable observations of Theobald Smith,[1] who has shown that the hæmocytozoön of Texas fever in cattle (*Pyrosoma bigeminum*) is conveyed from animal to animal by means of the cattle tick (*Boöphilus bovis*).

Experimentally it has been shown that although infection through the alimentary tract is improbable, subcutaneous infection is possible, while clinical observation is strongly in favor of the view that infection through the respiratory tract may occur.

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[1] U. S. Dept. of Agriculture, Bureau of Animal Industry, *Bull. No. 1*, Washington, 1892.

In Summary.—The malarial fevers flourish in low, moist, hot regions, the borders of rivers and marshes, places where the water is brackish being particularly dangerous. High, dry, sandy, or rocky regions are rarely malarious. In a malarious district there is greater danger of infection near the ground, by night than by day. There is suggestive evidence that the contagium may be carried by the winds. Age has no marked influence on the susceptibility. The negro is relatively much more insusceptible than the white. The manner of existence of the parasite outside the body and the manner in which the infection takes place are still wholly unknown.

PATHOLOGICAL ANATOMY.

(1) ANATOMICAL CHANGES IN ACUTE MALARIAL INFECTIONS; (2) CHANGES FOLLOWING REPEATED OR CHRONIC INFECTIONS.

Cases of the regularly intermittent fevers are so rarely met with upon the autopsy table that our knowledge of the pathological changes present in the internal organs are largely based upon a study of the cases of pernicious æstivo-autumnal fever. Our knowledge of the pathology of the malarial fevers has been greatly increased in late years by the investigations made since the discovery of the parasite by Laveran, Councilman and Abbott, Guarnieri, Dock, Bignami, Barker, and Monti. One of the most interesting points which at once strikes the careful observer is the extreme variation in the distribution of the malarial parasites in the body, and the anatomical changes produced by them in different cases. This difference in the localization of the parasites and in the seat of the important anatomical changes may bear, as has been pointed out in the description of the parasite, a direct relation to the symptoms which have existed during life.

The most striking point in the appearance of the organs in malarial fevers is the melanosis which gives a characteristic slaty gray color to many of the organs. This results from the accumulation of the pigment produced by the parasites from the hæmoglobin of the blood-corpuscles, and, while almost invariably present, its distribution, as in the case of the parasites, and the degree in which different organs are affected, varies considerably in different cases.

THE BRAIN.—The most striking changes in the brain are to be met with in the cases of comatose pernicious fever. The brain may be the seat of but few macroscopical changes. Melanosis may be entirely absent. At times, however, there may be a slight subpial œdema with hyperæmia of the cerebral substance, and perhaps punctate hemorrhages; more commonly, however, the gray cortex shows a slaty or chocolate color, which may be quite deep. The vessels are markedly injected, and in places, as has been said, punctate hemorrhages may be found. In these instances the microscopical appearances are most striking. The cerebral capillaries are crowded with parasites, which are, for the most part, within red corpuscles, and may form an actual complete injection of many of the cerebral vessels. This is generally most striking in the gray substance. These parasites (usually of the æstivo-autumnal type) may be in all stages of development, though generally one of the stages is most marked. Sometimes in cases where death has occurred during the paroxysm actual thrombi of segmenting organisms may exist. Sometimes the organisms may not be so numerous, but evidence of their previous existence is found in free clumps of pigment and swollen pigmented endothelial cells, as well as leucocytes containing pigment and red blood-corpuscles. There is usually decided granular and fatty degeneration, and often pigmentation of the endothelium of the vessels—a change upon which the punctate hemorrhages probably depend. Some endothelial cells may be greatly swollen, almost occluding the lumen of the vessels: these, as has been demonstrated, especially by Monti, may contain a considerable number of apparently well preserved parasites in various stages of development; they may be within shrunken or brassy corpuscles or full grown and free. Occasionally large macrophages are seen almost occluding the capillary, which appear, according to Monti, to be endothelial cells which have broken loose and are free in the current.

These lesions are particularly marked in the comatose form of pernicious malaria. In some instances different parts of the central nervous system may be differently affected. In one case, for instance, studied by Marchiafava,[1] where the patient died with symptoms of bulbar paralysis, a special localization of the changes was noted in the medulla. In other instances the cerebral lesions may be slight; the collections of parasites in the capillaries, as well as the degenerative changes in the endothelium, are not to be made out.

Monti[2] has recently studied the changes in the nerve cells in the gray cortex in pernicious malaria, according to Golgi's method, with interesting results. In some cases these elements were, so far as could be made out, quite normal, while in others interesting changes were noted: these cases were chiefly those showing grave nervous symptoms, such as coma, during life. The alterations were not uniformly diffused throughout the cortex, and never affected all the elements in a given zone. Usually cells more or less profoundly altered were found among other cells and fibres which were quite normal, although a tendency to a focal arrangement of these changes could be made out. The alterations affected chiefly the protoplasmic prolongations of the nervous cells of the cerebral cortex. Sometimes the prolongations appeared thinned and studded with fine nodes. Not infrequently these alterations were limited to the more delicate and distant branches, though it was not difficult to find cells of which all the dendrites presented the beaded appearance which is so well observed in the nerve cells of animals dead of inanition. In other points the alterations consisted of simple irregularities of contour in dendrites which were much thinned, extending from cells the bodies of which were sometimes normal, more often swollen, rarely thinned, shrunken, or atrophic. Coarser alterations were, however, not wanting. Cells were found whose dendrites showed coarse varicosities and very marked constrictions, so that they appeared as if formed of masses of protoplasmic matter connected only by the finest filaments of protoplasm. Similar changes were observed in the brains of animals in which embolisms were produced by the injection of lycopodium.

[1] *Lav. del. III. Cong. del. Soc. Ital. di Med. Int.*, Roma, 1890, 142.

[2] *Bull. d. Soc. Med.-Chir. di Pavia*, 1895.

In most of Monti's cases the axis cylinders were well preserved; the principal lesion appeared to consist in alterations of the protoplasmic prolongations. In some cases, however, especially in one severe case of comatose pernicious fever, certain alterations were to be made out in the axones. In this case the alterations of the nervous elements appeared more marked throughout the brain than in the other cases; the alterations in the dendrites were more frequent and marked, while the nervous prolongations also, had, in many points, lost their normal character. Instead of being smooth and regular as usual, they presented sometimes small nodes, more rarely larger swellings. Also, among the axones, as well in the cerebral cortex as in the cerebellum, there were occasionally varicosities. The alterations of the nervous fibres were, however, always less marked than those of the dendrites.

Monti believes that these changes are due to the grave circulatory disturbances, the occlusion of capillaries, lesions of their walls, the stasis, and the hemorrhages produced by the malarial parasites. It may be noted that many of these changes are not dissimilar to those described by Dr. Berkley in animals after the injection of ricin.

THE SPLEEN.—The spleen is always enlarged; there is a pronounced "acute splenic tumor." The capsule is tense. The parenchyma is cyanotic and sometimes is of a markedly slaty gray color; it is soft and is often almost diffluent. In acute malaria death may occasionally occur from rupture of an enlarged spleen. Microscopically, the pulp contains enormous numbers of red corpuscles, many of which contain parasites. These parasites may be in various stages of development. Sometimes, in the same organ, different areas show separate groups of parasites in different stages of development. Generally the pigmented and segmenting forms may be found in large numbers. Free forms of the parasite are relatively rare. One of the most striking appearances in the splenic pulp is, however, the presence of great numbers of phagocytes, some smaller and apparently leucocytic in nature, others very large cells, rich in protoplasm, containing a single large nucleus and occasionally a coarse granulation. These cells may reach an enormous size. They are laden with pigment, either in large clumps or spheres, in rodlets, or in very fine granules; the granules sometimes present the same arrangement which they had in the body of the parasite. The fine pigment may be distributed in delicate lines throughout the whole mass of protoplasm of the phagocyte; it often seems to vary in its color in different parts of the cell, but on focussing this appearance is found to be due to differences in plane. These large cells also contain red corpuscles, which are often partially or completely decolorized and contain parasites; and, finally, entire smaller phagocytes with their included pigment or corpuscles, as well as clumps of hæmoglobin of the color of old brass and fragments of degenerated red corpuscles. Golgi and Monti have called particular attention to the frequency with which these macrophages contain apparently well preserved parasites in different stages of development. They believe that the shrunken and brassy parasitiferous red corpuscles are engulfed in the phagocytes as would be any foreign body, while the included parasites continue their development within. Some of these macrophages may show evidences of necrosis. In some cases one may find in the pulp actual focal necroses, very much like those which may be seen in typhoid fever. These changes have been well described by Barker.[1]

There may be malarial pigment free in the intercellular spaces in the pulp. Pigmented polymorphonuclear cells are relatively rare; the small mononuclear elements and the lymphocytes of the follicles never contain pigment. The capillaries are usually filled with corpuscles containing parasites, while the splenic veins show relatively few, though they always contain phagocytes containing pigment and fragments of blood-corpuscles.

THE LIVER.—The liver is often of an intense slaty gray color, which depends upon the enormous numbers of parasites and of pigment contained in the capillaries. The distribution of the pigment is different, as will be pointed out later, in this acute malarial infection from that characteristic of repeated attacks. There is always a marked cloudy swelling. Microscopically, the capillaries are often crowded with leucocytes and contain numerous phagocytes; some of the largest macrophages are here observed. Not infrequently the endothelial cells may be also observed to show evidences of phagocytic action. The perivascular tissue in the portal spaces may show numerous pigment bearing cells, while frequently liver cells may be found to contain clumps of pigment derived from the blood and altered red corpuscles. This condition, similar to that observed in pernicious anæmia, accounts, doubtless, for the polycholia and the subicteric hue so commonly observed in the malarial fevers. Ordinarily relatively few parasites within red corpuscles are to be found within the vessels: these are more numerous in the interlobular branches of the portal vein. In the intralobular veins one more often sees the macrophages.

Among the most interesting changes to be noted in the liver are occasionally occurring disseminated areas of local necrosis of the liver elements with fragmentation of the nuclei, wandering in of leucocytes, and sometimes with evidences of proliferation of cells in the surrounding tissue. These changes are very similar to those already noted in typhoid fever and other acute infectious diseases, and proven by Welch and Flexner[2] to be produced in diphtheria, and by Reed[3] in typhoid fever, by a circulating toxic substance. The occurrence of these foci in the liver was first described by Guarnieri,[4] who ascribed them to the cutting off of the nutrition by the extensive blocking of the intralobular capillaries with pigment bearing phagocytes. Barker[5] describes and pictures capillary thromboses in association with many of these areas.

THE LUNGS.—The alveolar capillaries show, generally, large numbers of phagocytes, which are, however, smaller than the largest macrophages of the liver and spleen. Their substance may show evidence of necrosis. Occasionally pigment may be found in the endothelial cells of the capillaries and small veins, but much more rarely than in the capillaries of the brain or of the liver. Leucocytes containing malarial pigment are seldom found in the interior of the alveoli. Mononuclear phagocytes are much more frequent than ordinary polymorphonuclear leucocytes, which, when present, contain, usually, finer, smaller particles of pigment. The macrophages are generally collected about the periphery of the smaller veins. The endoglobular parasites show, usually, all stages of development. The endothelium of the capillaries and small veins rarely contains pigment, in sharp contrast to the condition existing in the brain. It is striking that the areas of bronchopneumonia, which are not infrequently found, contain only the ordinary polymorphonuclear leucocytes and alveolar epithelial cells, pigmented elements being very rarely present. The capillaries of the septa may, however, be filled with pigment and macrophages. Bignami suggests that this fact is due to the diminished vitality of the pigment bearing cells, which have, to a certain extent, lost their motile power and are thus less able to pass through the vessels.

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[1] *Johns Hopkins Hospital Reports*, vol. v., 1895.

[2] *The Johns Hopkins Hospital Bulletin*, No. 20, March, 1892.

[3] *Johns Hopkins Hospital Reports*, vol. v., 1895.

[4] *Atti della R. Acc. Med. di Roma*, 1887, s. ii. v. iii. 247–266.

[5] *Loc. cit.*

THE KIDNEYS.—The changes in the kidneys in acute malaria are usually much less marked than in the liver and spleen. Their gross appearance varies but little from the normal. Evidences of pigmentation are usually wanting on gross examination. The malarial parasites and phagocytes are usually present in smaller numbers, the quantity being disproportionately small in comparison to the alterations of the parenchyma which are sometimes to be found. The glomeruli, however, are ordinarily considerably pigmented, the pigment at times being seen within large white cells within the vessels, sometimes in the glomerular endothelium. Endoglobular parasites are rarely seen in the capillaries of the glomeruli; they are more common in the intertubular vessels, but are rare even there. The most important lesions consist in exfoliation and degeneration of the epithelium lining the capsules. Albuminous exudates within the glomeruli were found by Bignami only in algid pernicious fever. At times, however, there may be marked alterations in the parenchyma—to wit, focal necroses of the epithelium, especially that of the convoluted tubules.

The changes in the kidneys in cases of hæmoglobinuric fever have been described by Pellarin,[1] Benoit,[2] Kiéner, and Kelsch.[3] The kidneys are somewhat increased in size, the color varying from a deep reddish brown to a light yellowish brown coffee color in more anæmic individuals. When the color is pale, irregular pinhead points and blotches of a maroon color are to be seen upon the surface, some as large as several millimetres in area. They are also scattered throughout the cortex. These have been shown by Kelsch and Kiéner to be due to pigment deposits; they are not visible in more congested kidneys. The pyramids are of a deep red color from intratubular hemorrhages. The capsule is easily detached; the consistency of the gland is normal.

Microscopically, the epithelium of the convoluted tubules and of the large branches of Henle's loops are very opaque, the nuclei being scarcely visible. This is due to an infiltration of the protoplasm with a diffuse coloring matter and fine pigment granules which are rendered more evident by KOH. These granules are extremely small, and separately appear of a yellowish color, while *en masse* they have a brown shade. The epithelial cells are swollen and bulge into the lumen of the canal. Occasionally a cell shows a hyaline protrusion which seems on the point of escaping. In some tubes the epithelial covering is represented only by a thin protoplasmic layer with a homogeneous surface, appearing as if eroded down to the level of the nuclei. The lumen of the tubule is filled with clumps of amorphous material or casts mixed to a greater or less extent with this pigment. The brown specks and blotches seen macroscopically represent groups of tubules, the epithelium and lumina of which are crowded with similar masses of pigment; but pigment may also be found in larger granules—granules nearly as large as a red blood-corpuscle, and more or less spherical; they are refractive, of a color varying from a yellow ochre to a deep brown, and are sometimes accumulated in epithelial cells which bulge so as to almost occlude the lumen. Sometimes they occupy the lumen and form conglomerations, taking the shape of casts; sometimes they are fused into a vitreoid mass. Between the opaque dark casts formed by the fine brown granulations and the almost vitreoid casts composed of the large orange colored granulations every intermediate stage may be seen in the same preparation. Generally this pigment gives no reaction for iron, though Kelsch and Kiéner have obtained this reaction from certain granules in one case. The finely granular substance is found, according to these authors, more particularly in cases where death has occurred in a pernicious paroxysm, while the larger forms of pigment are more frequent in cases of longer duration. In the glomeruli, as well as in the blood, Kelsch and Kiéner have never seen the large variety of granules, though the finer granules are numerous. Between the glomerulus and capsule, usually near the mouth of the tubule, there is often quite a collection of granules, which are also found sometimes in epithelial cells, sometimes free. In the glomerulus itself one may see fine granulations disseminated in its substance and apparently included in the cells of the capillary walls. More rarely granulations may be accumulated in a capillary loop. In some cases there are small interstitial hemorrhages. The pyramids show few changes. The same varieties of casts as noted above may be found, and the same pigment collections. The epithelium is usually intact, though sometimes protruding and vesicular cells suggest that they may take part in the formation of hyaline material. Almost invariably a number of the tubes are found filled with blood-corpuscles.

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[1] *Arch. de Méd. nav.*, 1865.

[2] *Ibid.*

[3] *Arch. de Phys.*, 1882.

THE GASTRO-INTESTINAL TRACT.—The stomach and intestines show, under ordinary circumstances, few changes beyond the melanosis. It is to be remembered, however, that the intestinal mucous membrane may be of a dark steel gray color in conditions other than malaria. Microscopically, one may see a considerable number of parasites, especially of the full grown and segmenting varieties, in the capillaries of the mucous membrane, together with numerous pigmented cells and apparently few pigment clumps. In most cases, however, the gastro-intestinal mucous membrane is not particularly sought by the parasites.

In other instances, as pointed out by Marchiafava and Bignami, this region may be the seat of the main localization of the affection. Macroscopically, there may be intense hyperæmia with punctate hemorrhages in the gastro-intestinal mucosa. In one instance observed by the author there was a distinct dusky slaty tinge as well. Here the capillaries throughout the gastro-intestinal tract may be crowded and blocked with parasites, free and contained in the red corpuscles or in phagocytes. As in the case of the brain, actual thromboses may exist with necrosis of the epithelial covering and ulceration. Cases of this nature are associated frequently with marked gastro-intestinal symptoms, some showing a clinical picture very similar to that of Asiatic cholera.

THE BONE MARROW.—The marrow is generally of a dark slaty color; it is often almost black. The small vessels are filled with endoglobular pigmented parasites, while numerous macrophages containing pigment and red blood-corpuscles may be found about the periphery of the lumina of the vessels. At times, between the corpuscles, Bignami[1] found numerous ovoid or round bodies which, from their size and staining propensities, he believed to be free spores. Not only in the vessels, but also outside of these, the parasites are to be found in greater or less number. The macrophages are, however, especially numerous, even in the pulp. At times also free pigment clumps are apparently to be made out.

The ADRENAL GLANDS may be the seat of pronounced alterations. There are irregular areas of vascular dilatation, parasites being numerous in the distended vessels. Macrophages with varying contents may be present in considerable numbers. The endothelial cells of the vessels may be phagocytic, and malarial pigment and infected corpuscles may even be enclosed by true adrenal cells.

In the other organs there is little that is characteristic.

(2) CHANGES FOLLOWING REPEATED OR CHRONIC INFECTIONS.—CHRONIC MALARIAL CACHEXIA.

While the above mentioned changes are found in the acutely fatal cases of malaria, interesting pathological changes may occur in various organs as the result of long continued or frequently repeated attacks. The most important of these changes occur in the spleen, the liver, the bone marrow, and the circulating blood.

THE SPLEEN.—The spleen is always considerably enlarged; it may be enormous, reaching beyond the umbilicus and as low as the pubes. It is firm and hard; the border is sharp. The capsule is usually much thickened, and white fibrous cartilaginoid plaques occur upon the surface. On section it has often a somewhat slaty color, while the trabeculæ are very prominent.

The minute anatomy and development of the changes in the viscera, following repeated malarial attacks, has been followed with particular care by Bignami,[2] upon whose valuable work we shall largely trespass in the following description. The acute splenic tumor is caused chiefly by the aggregation in the pulp of the spleen of an enormous number of red corpuscles which have become either shrunken and brassy colored or decolorized, and are found included in the colorless elements of the spleen as brassy colored fragments or hyaline masses; by the continuous aggregation of colorless elements containing pigment, red corpuscles, or parasites, which collect from all parts of the body, and many of which are necrotic; and, thirdly, by great numbers of red corpuscles containing parasites, some of which apparently pass through the vessel walls by diapedesis and seek the columns of the pulp, where they are for the most part enclosed by the epithelioid elements. While, as a result of this proceeding, a considerable number of the proper elements of the spleen become necrotic, others, as well in the pulp as in the follicles, undergo karyokinetic division, while all this is followed by a marked hyperæmia and acute tumor of the splenic pulp. Thus the spleen is converted into a place for the deposit of cadavers, while at the same time, during the same infection, processes of regeneration have begun to appear.

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[1] *Atti d. R. Acc. Med. di Roma*, Anno xvi. v., 1890.

[2] *Bull. d. R. Acc. Med. di Roma*, 1893, Anno xix. f. 4, p. 186.

When the actual infection is at an end and the acute hyperæmia of the spleen has ceased, the tissues in the neighborhood of these collections of necrotic elements, or those surrounding the necrotic areas of the splenic pulp, show certain changes which, on the one hand, tend to produce permanent alterations, and on the other to lead to a partial reparation of the part. In those parts where a considerable portion of the splenic tissue becomes necrotic or disappears, being carried away by the lymphatics, the splenic vessels become considerably dilated, forming a network of venous lacunæ which are separated by thin layers of pulp. This results in a tissue simulating that of an angioma. In those cases where a more marked destruction of the splenic tissue has occurred, and where every trace of the pulp is gone, parts become represented by extensive areas of tissue which consist of wide cavernous sinuses, the septa of which are composed of a very delicate connective tissue, rich in giant cells, similar to that of the bone marrow. Some of the follicles become necrotic and fibrous. While this occurs a process of regeneration yet more extensive takes place, starting for the most part from the follicles, but also sometimes from the splenic pulp. The follicles become hyperplastic, reaching sometimes three or four times their normal size. This new form of lymphoid tissue, starting from the follicles, may be sometimes seen to surround necrotic areas of splenic tissue which become smaller and smaller and finally disappear. In the neighborhood of these hyperplastic follicles occurs a hyperplasia of the true elements of the pulp, while the reticulum becomes thickened so as to give rise, in preparations, to very beautiful and clear figures, such as are not to be seen in the normal spleen. The pigment and probably the greater part of the necrotic elements are carried on toward and collected about the periphery of the follicles, so that the diffuse melanosis of the pulp is followed by a perifollicular melanosis. The pigment then passes on into the lymphatic vessels of the sheaths of the arteries and of the connective tissue of the septa. This results, on the one hand, in thickening of the vascular sheaths and of the septa, and, on the other hand, in the appearance of single or multiple lymphatic cysts, giving sometimes the picture of a lymphangioma and resulting in chronic lymph stasis.

When we consider that after each new infection fresh processes similar to these must occur, it is easy to understand the gradual development of the enormous splenic tumors, in which, sometimes, it is difficult, even histologically, to recognize the original structure of the organ.

THE LIVER.—The changes occurring in the liver in chronic malaria may in the same manner be traced from those occurring in the acute infection. In the acute infection an enormous number of phagocytes, pigmentiferous or globuliferous, coming in great part from the spleen, invades the capillary network of the liver, while the parasites are generally scanty. The circulation is slowed, the capillary network becomes dilated, while a certain amount of pigment is taken up by the endothelial cells of the vessels, and later by Kupffer's cells. The pigmented endothelium becomes swollen and in part necrotic. These vascular changes are followed by new areas of blood stasis. At the same time, as has been noted, many of the liver cells suffer alterations, either undergoing an acute atrophy from pressure or a coagulative necrosis. These areas are sometimes quite extensive. In other instances many cells are found to be filled with blocks of yellowish iron-containing pigment, resulting from the early death of many red corpuscles. At the same time a certain number of liver cells, Kupffer's cells, and endothelial cells multiply by karyokinesis. The result of all this is the acute hepatic tumor and the increase in functional activity—polycholia.

But a small part of the great number of pigmented elements which enter the liver escape, passing through the branches of the suprahepatic veins. The greater part is taken up by endothelial and perivascular cells, so that the melanæmia is followed by a melanosis of the vessels. The pigment then passes forward out of the capillary network into the perivascular lymph channels, where it is collected in large blocks enclosed in white cells. These carry the pigment following the lymph channels to the periphery of the lobules, and perilobular melanosis follows thus the interlobular melanosis. This process then extends, and the masses of pigment are to be found three or four months after the end of the infection in large blocks, for the most part endocellular, in the perivascular lymphatic tissue of Glisson's capsule.

While this migration of pigment is going on in the lobule there occur, on the one hand, permanent alterations, and on the other hand regenerative processes. Where the dilatation of the lymph and blood-vessels and the degeneration and pigmentation of the vascular elements is most marked and extensive, no regeneration may follow the atrophy and necrosis of the endothelial and liver cells. The dilatation of the vessels increases and becomes permanent. The greater part of the remaining liver elements disappears; only a few remain in an atrophic condition, the tissue showing an angioma-like appearance consisting of ectatic vascular network, about which may be recognized a stroma consisting of Kupffer's cells. Where the dilatation of the lymph vessels is most marked there may occur small lymphatic cysts.

In all parts of the liver, when the normal blood current has been restored after the disappearance of the pigment and the necrotic masses in general from the endothelial cells of the vessel walls, an active regeneration of the tissue elements occurs about the atrophic or necrotic liver cells. The young hepatic cells become arranged with great regularity in long rows on both sides of the old elements. Thus, when the stroma remains intact, an interlobular regeneration may occur. These regenerative processes are accompanied by the appearance of giant cells with budding nuclei, just such as are found in the embryonic liver. The regeneration never appears in parts of the liver that have not been entirely freed from the collections of pigment and parasites.

The migration and collection of the pigment in the perilobular tissue is followed by a hyperplasia of this tissue, so that the surroundings of the lobules are more distinct. These de- and regenerative changes result, then, in a marked increase in the size of some lobules and a diminution in size and an atrophy of others. As this process accompanies each acute infection, one can readily understand the chronic perilobular, monolobular hepatitis of malaria, which is characterized by the presence of zones of hyperplasia or of atrophy of the parenchyma, by chronic blood and lymph stasis, by the formation of areas of angiomatoid tissue, by lymphectases and lymphatic cysts. In this manner the large liver tumors which are so well known, with smooth surface and lobules of irregular size, have their origin.

Bignami divides the processes in the liver into four stages:

(1) The liver appears congested, while the lobules are not sharply distinguishable and show in severe cases a decreased melanosis. The macroscopical characters are about the same as those of the liver in acute malarial infections. Microscopically, at this period, a little after the termination of the acute infection, it may be noted that the parasites have disappeared from the capillaries of the liver, the pigmented endovascular macrophages have in great part gone, and the pigment is entirely collected in the endothelium and in Kupffer's cells. Those parts of the hepatic lobules in which necrosis or degeneration has occurred undergo a marked atrophy; the necrotic and degenerate elements are carried away in the phagocytes, while the vascular network becomes dilated.

(2) In a more advanced stage on gross examination the lobules are distinct. The melanosis continues to be diffuse throughout the lobule, but is more marked at its periphery. The organ is still congested. The particular features of this stage are that, on the one hand, the hepatic lobule frees itself from the accumulation of pigment and the necrotic remains, which become collected toward the periphery of the lobule, while, on the other hand, an active process begins which tends toward a partial regeneration of the parenchyma.

(3) In this stage the diffuse melanosis of the lobule, with the greater prevalence of pigment toward the periphery, is succeeded by an exclusively perilobular melanosis. The liver is enlarged, the consistency somewhat increased, the surface smooth. On section one may see that all the lobules are surrounded by a slate colored line, in the neighborhood of which the coloration of that part of the lobule is somewhat brown. In general, the slaty lines marking out each lobule form an exquisite network. The size of individual lobules varies greatly: some are two or three times the normal size, others are markedly diminished. Microscopically, it may be observed that the degenerative alterations of some lobules have led to the formation of false angiomata and of lacunæ or cysts of lymphatic nature. Other lobules, by the process of regeneration already described, have increased notably in volume. The pigment has become extravascular; its transport through the capillaries and perilobular lymphatics is brought about by white mono- and polymorphonuclear cells.

(4) In cases in which the acute infection has passed for several months (in one case three months only) the pigmentation is greatly diminished and scarcely visible to the naked eye. The liver is notably enlarged and congested. The surface is smooth. On section one may see the lobules distinctly marked, surrounded by a most delicate red-

dish brown border; the consistency is somewhat increased. Microscopical examination shows that the melanosis has become exclusively perivascular.

(5) Lastly, one arrives at the definite terminal form of the chronic malarial hepatic tumor. The macroscopical characters are the following: The liver is increased in size and in weight, sometimes enormously; the surface is smooth, the capsule a little thickened. On section the appearance is finely granular, the lobules are distinct, a little prominent, and surrounded by a zone of slightly pinkish tissue. Microscopical examination shows the disappearance of all malarial pigment. The alterations of the parenchyma are similar to those described in the last two stages. The lobules of varying size are surrounded by a hyperplastic perilobular connective tissue. The connective tissue of the larger septa is, on the other hand, of about normal volume. A notable dilatation of the capillaries, with stasis of the colorless corpuscles, persists. The hepatic cells are altered in form in the zones where the dilatation is most marked. There is considerable difference in individual cases in the extent of these various lesions. There are cases, for example, in which, despite the enormous increase in the weight of the organ, there may be no very marked dilatation of the capillaries, nor are false angiomata or lymphatic cysts to be found, while, on the other hand, the hyperplasia of the perilobular connective tissue and the increase in volume of many lobules may be more marked: there may be an evident hyperplasia of the parenchyma (hepatic cells with many nuclei and nuclei rich in chromatic substance). In other cases, on the other hand, the cysts and false angiomata may be enormously developed, so as to constitute one of the chief factors in the enlargement of the liver.

THE BONE MARROW.—In individuals who have had numerous relapses of malarial fever the marrow of the long bones—for example, of the femur in the upper and lower fourths—is usually red and of a consistency greater than is generally seen in acute infections. The microscopical alterations are various; generally the signs of an active proliferation of the proper elements of the marrow are present. This leads to an increase in the hæmatopoietic activity. There are factors, however, such as the degenerative and destructive alterations which take place in the bone marrow during acute infections, which injure, to a varying extent and through a varying length of time, the hæmatopoietic functions of the marrow. In other cases, very rare indeed, the bone marrow presents the macroscopical and microscopical features which exist in acute pernicious anæmia, particularly the presence of a considerable number of megaloblasts. Lastly, there may be cases in which the new formation of the hæmatoblastic marrow is wanting or entirely insufficient. In these cases the post-malarial anæmia is of necessity progressive.

THE BLOOD.—Corresponding to the change in the bone marrow, Bignami and Dionisi[1] distinguish four types of post-malarial anæmia:

(1) Anæmiæ in which the examination of the blood shows alterations similar to those observed in secondary anæmiæ, from which they differ only in that the leucocytes are diminished in number. The greater part

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[1] *Cent. f. Allg. Path. u. Path. Anat.*, 1894, V. No. 10, 422.

of these cases go on to recovery; a few, without any further change in the hæmatological condition, pursue a fatal course.

(2) Anæmiæ in which the examination of the blood shows alterations similar to those seen in pernicious anæmia—presence of gigantoblasts (megaloblasts). These cases end fatally.

(3) Anæmiæ which are progressive, as a result of lack of compensation by the marrow for losses brought about by the infection. At autopsy the marrow of the long bones is found to be wholly yellow, while the marrow of the flat bones is also poor in nucleated red corpuscles.

(4) Chronic anæmiæ of the cachectic, which differ from the above-mentioned types by clinical and anatomical characters in that the special symptoms of malarial cachexia prevail, while one observes post-mortem a sort of sclerosis of the bone marrow. The marrow of the long bones is red and of an increased consistency; the giant cells are very numerous, and many are necrotic; the nucleated red blood-corpuscles are very rare, and the colorless polymorphonuclear corpuscles are present in small numbers.

THE KIDNEYS.—The kidneys in chronic malaria show usually no great changes. Kiéner, however, describes two forms of kidneys met with in chronic paludism: (1) the congested form, and (2) the atrophic form.

(1) The engorged kidneys are voluminous, increased in weight; the surface is smooth, the consistency firm, the color of a deep red. The congestion is especially marked in the pyramids. All the vessels are distended, and the congestion is sometimes so extreme that interstitial hemorrhages may result or hemorrhages into the interior of the tubules. The epithelium of the tubules is granular; there is often desquamation, and hyaline casts may be found.

(2) The atrophic kidneys are small and irregular in surface. The capsule is adherent, the consistency increased. The kidneys show a maroon or mahogany color or a blotchy appearance. Small cysts are often to be found. The microscope shows alterations as well in the connective tissue as in the epithelium of the tubules.

Amyloid degeneration occasionally follows chronic malaria. This has been noted in the kidneys by Laveran[1] in two instances, but in both of them the malarial cachexia was complicated with chronic broncho-pneumonia and bronchiectasis. Frerichs[2] describes three cases, while Marchiafava and Bignami[3] have carefully studied several instances. The clinical history of these cases showed that after a long period of febrile attacks (æstivo-autumnal or obstinate quartan) there followed the symptoms of nephritis and a rapid cachexia, in which the patients died in a few months. On autopsy the principal changes that were found were a grave anæmia, a marantic condition of the organs, a chronic nephritis, and a diffuse amyloid degeneration. The distribution of the amyloid substance in their cases was as follows: The degeneration was most prevalent in the *kidneys*, where not only the vessels of small and medium size and glomeruli were affected, but also, to a considerable extent, the walls of the renal tubules. The alteration of the interstitial tissue and the degenerations of the renal parenchyma are very grave.

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[1] *Traité des Fièvres palustres*, p. 94.

[2] *Lehrbuch der Leberkrankheiten.*

[3] *Riforma Medica*, 1891, vol. i. p. 571.

After the kidneys the amyloid degeneration is most severe in the *intestines* and the *spleen*. In the *intestine* the degeneration affects chiefly the vessels of the villi, but also the vessels of the submucosa, and to less extent those of the other intestinal coats. In the *spleen* the vascular network of the periphery of the follicles is particularly affected. Here one sees usually the deposition of great blocks of amyloid substance, while in the trabeculæ of the pulp the process is in its beginning or is entirely wanting. In the *liver* there is a less extensive and diffuse deposition of amyloid substance than in the kidneys. The degeneration affects islands of hepatic tissue which are irregularly disseminated, so that, for example, one may see an island of the size of a lobule or larger from which the hepatic tissue has entirely disappeared, the vascular network showing a most grave amyloid degeneration, while about this the hepatic tissue has a normal appearance. The first small zones of degeneration, according to Bignami, seek by preference the periphery of the hepatic lobules, from whence the process spreads.

MALARIAL CIRRHOSIS.—THE RELATION OF CHRONIC OR REPEATED MALARIAL INFECTIONS TO CIRRHOTIC PROCESSES.

For many years certain authors have associated cirrhosis of the liver, certain chronic renal changes, and, in some instances, chronic inflammation of the lung, endocardium, and central nervous system, with malarial fever. Indeed, in almost all works upon medicine malarial fever is included as one of the etiological factors in ordinary atrophic cirrhosis of the liver. This statement has been based almost entirely upon rough clinical observation, no one having definitely traced the development of the cirrhosis from the changes following acute or chronic malaria. Frerichs[1] noted the rarity of cirrhosis in patients dying with chronic malaria, though in five instances this was the only etiological cause which he could discover. Laveran[2] in his considerable experience has seen but two cases of atrophic cirrhosis following malarial fever. Welch has seen but one case of atrophic cirrhosis which appeared to follow malaria.

Kelsch and Kiéner give a longer description of hepatitis in malaria, distinguishing three forms of chronic malarial hepatitis and two groups of malarial cirrhoses: (1) Insular cirrhosis with nodular hepatitis and insular cirrhosis with diffuse parenchymatous hepatitis; (2) annular cirrhosis with nodular or diffuse parenchymatous hepatitis. The general appearance of the liver in these cases is that of ordinary atrophic cirrhosis.

Bignami has recently discussed this subject in a very thorough manner. He concludes that there is little evidence to show that ordinary atrophic cirrhosis is a frequent follower of malarial fever. After describing the development of the ordinary chronic hepatic tumor of malarial cachexia, he says: "It is easy to understand from this that it is not difficult to make a differential diagnosis between this form of chronic tumor—or of chronic hepatitis, as one might say—from the other forms of cirrhosis. There are not facts or reasons sufficient to cause us to believe that ordinary cirrhosis can follow a chronic tumor. The structure in the two cases is absolutely different. In the one we have an extensive new formation of connective tissue, multilobular in nature, retracting about the included lobules; in the other, a more scanty formation of perilobular connective tissue about a single lobule, not contracting, together with grave alterations of the lobules themselves, especially of their vascular and lymphatic system, not depending, as we have seen, upon the new formation of perilobular connective tissue, but due to lesions primarily local. Atrophic conditions of the liver exist in malaria, but are simple atrophies, and occur in patients who are exhausted, for example, by profuse diarrhœa, etc., or in cases which I have described as progressive post-malarial anæmia. They depend upon the complete want or almost complete absence of any process tending toward regeneration, resulting from grave and diffuse regressive alterations."

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[1] *Loc. cit.*

[2] *Traité des Fièvres palustres*, p. 90.

Barker[1] has recently ably discussed the relation of malarial infections to cirrhotic processes, and has emphasized the fact that many conditions exist in the organs in malarial fever which might well be the starting-point for extensive growth of connective tissue. Flexner,[2] after the injection of blood serum from one animal into another, has seen the development of characteristic cirrhosis of the liver and of the kidneys in rabbits, following focal necroses not dissimilar to those found in the liver in acute malarial infections.

In conclusion, then, it may be said that secondary sclerotic processes of greater or less degree in the liver, spleen, and bone marrow are not uncommon after repeated malarial infections. The question of the possibility of the development of a *true atrophic cirrhosis* of the liver, of malarial origin, is not settled; the development has never been actually traced and the condition, if it exist at all, is probably rare. The possibility of its occurrence cannot, however, be denied.

SYMPTOMS.

PERIOD OF INCUBATION.—In the absence of definite knowledge as to how malaria is acquired, the ideas concerning the period of incubation have varied very greatly. It has undoubtedly been observed that characteristic malarial fever may appear very shortly after exposure in a malarious district, many observers believing that this may occur within a shorter time than twenty-four hours. It is possible that the febrile attacks which occur sometimes immediately after exposure at night in damp, marshy, malarious districts may have some other cause than malarial infection. Thus, Plehn describes cases where, after exposure at night in very malarious districts in West Africa, there was an immediate paroxysm similar to a malarial attack, which, however, did not recur until the appearance, ten days later, of a true malarial fever, which doubtless dated its infection from the night of exposure. At the time of the first paroxysm the blood was negative, the parasite (æstivo-autumnal) not appearing until ten days later. The hypothesis of Plehn that the initial paroxysm was due to the absorption of some toxic substance produced, perhaps, by the parasite outside of the body, is ingenious, but seems a little far-fetched. More commonly an interval of one or two weeks may be made out between the time of exposure and the time of the breaking out of the disease. Maillot[1] considered the mean period of incubation to be from ten to twelve days, while Sorel[2] estimated it at from seven to nine days. Hertz[3] states that the period of incubation is commonly reckoned at from six to twenty days, but believes that the disease may appear immediately after the reception of the injurious influence.

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[1] *Johns Hopkins Hospital Reports*, vol. v.

[2] *The Medical News*, Philad., Aug., 1894.

A number of instances of prolonged incubation have been reported, many of which are open to doubt. Some of these, however, are hard to explain. Such, for instance, is the case of Blaxall,[4] where, after spending five days in the harbor of Port Louis, two of the crew of a man-of-war were attacked, at the end of, respectively, twelve and fourteen days, with quotidian intermittent fever, while two others developed tertian fever at the end of, respectively, forty-eight and one hundred and eighty-four days after embarkation. It is probable, in view of our present knowledge, that many cases of prolonged incubation represent relapses of earlier attacks, the manifestations of which have been present and would have been evident on more careful examination.

Of recent years, since the discoveries of the malarial parasite and the inoculation experiments of Gerhardt,[5] Mariotti and Ciarrochi,[6] Marchiafava and Celli,[7] Gualdi and Antolisei,[8] Angelini,[9] Di Mattei,[10] Calandruccio,[11] Bein,[12] Baccelli,[13] Sacharov,[14] the subject has been considered in a much more intelligent manner. The period of incubation in these cases where the blood of one malarial patient was introduced intravenously or hypodermically into a healthy individual, have varied greatly. In individual cases there was a variance in the period of incubation of from six to eighteen days, while the average duration was from eleven to twelve days. Recently, Bastianelli and Bignami[15] have contributed four new cases to this list and have made a careful study of this subject. In their words, the period of incubation in these cases of artificial inoculation represents "the time necessary for the inoculated parasites to arrive, by multiplication, at the quantity necessary to determine the fever." . . . . "The period of incubation with a given variety of parasites varies inversely to the quantity of material inoculated." . . . . "The mean and minimum period of incubation under equal conditions varies with the various groups of the fever: it is least with æstival fevers, a little longer with tertian fever, and yet a little longer with quartan fever." They believe that they are justified in concluding that "the period of incubation in experimental malarial infections is not a constant quantity, but varies in the same group of fevers and in different groups. In a given group of fevers it depends primarily upon the quantity of material inoculated. In different groups of fevers it varies with the rapidity of the cycle of development of the parasites and with the special capacity for reproduction of the parasitic variety."

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[1] *Traité des Fièvres*, p. 263.

[2] *Arch. de Médecin milit.*, 1884, t. 3, p. 273.

[3] *Ziemssen's Cyclopædia*, vol. ii. p. 588.

[4] Quoted from Hertz, *loc. cit.*

[5] *Zeitschr. f. klin. Med.*, 1884, 375.

[6] *Lo Sperimentale*, 1884, s. iv. t. liv. 263.

[7] *Fortschritte d. Med.*, 1885, iii. Nos. 11 and 14.

[8] *Rif. Med.*, 1889, Nos. 225, 264, 274.

[9] *Rif. Med.*, 1889, Nos. 226 and 227, pp. 1352, 1358.

[10] *Ibid.*, 1891, p. 544, and *Arch. für Hyg.*, 1895, 191.

[11] Cf. Grassi and Feletti; *Cent. für Backt.*, 1891, ix. 403, 429, 461.

[12] *Charité Annalen*, 1891, 181.

[13] *Deutsch. med. Woch.*, 1892, No. 32, 721.

[14] *Cent. für Backt.*, 1894, xv. p. 158.

[15] *Bull. d. R. Acc. Med. di Roma*, 1893–94, Anno xv., v. xx. 151.

They have constructed the following table from an analysis of all cases of experimental malarial infection which they could collect:

Period of Incubation.	Maximum (days).	Minimum (days).	Mean (days).
Quartan fever	15	11	13
Tertian fever	12	6	10
Æstivo-autumnal fever	5	2	3

These researches, especially those of Bastianelli and Bignami proving that the incubation period in æstivo-autumnal fever may be as brief as two days, are of a great deal of interest. It is striking to see how well their conclusions agree with the deductions which have been drawn by other observers before the discovery of the malarial parasite. It is with the æstivo-autumnal variety of the parasite, that variety which is associated with the pernicious fevers, that the short periods of incubation have been observed, while the older clinical observations of short periods of incubation relate usually to the same class of cases. We cannot, however, positively assume that these figures represent the period of incubation in infection as it ordinarily takes place, for we do not know how or in what form this occurs.

The general results, however, of inoculations in tertian and quartan fevers agree quite closely with what might have been expected from clinical observation, while the demonstration that after small intravenous inoculations in æstivo-autumnal fever the disease may appear in forty-eight hours makes it very easy for us to believe that, however the infection may occur, the true incubation period in some very malignant fevers may be extremely short.

Plehn[1] advances an ingenious hypothesis to account for certain early manifestations of fever. He asserts, as has been stated above, that he has noticed in several instances a well marked febrile reaction occurring within a few hours after exposure in a malarious locality and simulating a single malarial paroxysm. The examination of the blood was negative. From nine to twelve days later, however, characteristic malarial fever developed, the parasites being readily found in the blood. He suggests that by exposure in extremely malarious districts the individual may absorb a sufficient quantity of a pyrogenic toxine to cause immediately a single paroxysm days before the true incubation period has been passed through; there is, however, little which can be advanced as proof of such an hypothesis.

Basing our conclusions, then, upon the comparison between clinical deductions and the accurate observation of inoculation experiments, we may say that it seems likely that the ordinary period of incubation in tertian fever is about ten or twelve days, in quartan fever a little longer, while in æstivo-autumnal fever the period may range from twenty-four hours or even less to ten days or two weeks, averaging probably a somewhat shorter time than in the case of tertian or quartan fever.

TYPES OF FEVER.—The malarial fevers may be divided into two main classes: (1) The regularly intermittent fevers, occurring throughout the malarial season; (2) the more irregular, often more or less continued fevers, occurring in temperate climates, only at the height of the malarial season, the late summer and early fall.

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[1] *Virch. Archiv*, 1892, cxxix. 285.

And under these two main classes one may separate three distinct types of fever, depending in turn upon infection with one of the three types of the malarial parasite which have been described previously. Thus, the first class, the regularly intermittent fevers, includes (*a*) *tertian fever*, with its combinations (double tertian fever), and (*b*) *quartan fever*, with its combinations (double and triple quartan fever). The second class of fevers, that including the more irregular varieties, depends upon infection with the third variety of parasite above described. Occurring, as it does, at the height of the malarial season (August, September, October), it justly deserves the name (*c*) *æstivo-autumnal fever* applied to it by the Italian observers.

Tertian fever is common in almost all malarial regions. Quartan fever is, however, rare in many districts where the other forms of infection are frequent. In the United States quartan fever appears to be rare; in the last seven years, out of nearly a thousand cases observed at the Johns Hopkins Hospital, only nine cases of quartan fever have been seen. On the other hand, there are certain regions in which quartan fever is particularly common, as the neighborhood of Pavia in Italy and in certain parts of Sicily.[1]

These types of fever are the same wherever they exist. In tropical countries the severer types of æstivo-autumnal fevers are in excess. As one passes away from the equator only the milder tertian and quartan fevers are to be seen in the earlier part of the malarial season, while the æstivo-autumnal fevers appear in the later summer and early autumn. Lastly, in districts where malaria is very uncommon the milder forms, tertian and quartan fever, alone prevail.

TERTIAN FEVER.—(1) *Single Infections—Tertian Intermittent Fever;* (2) *Double Infections—Quotidian Intermittent Fever.*

(1) *Single Infections—Tertian Intermittent Fever.*—This type of fever depends upon infection with the tertian parasite, an organism which, as has been described, possesses the remarkable characteristic of existing in the blood of the infected individual in great groups, all the members of which are approximately at the same stage of development and pass

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[1] The interesting fact that districts closely adjoining one another and presenting the same general physical conditions may be each the *foyer* for a distinct type of malarial fever was noted by Trousseau some years before the discovery of the parasite. In discussing the types of regularly intermittent fevers the great clinician says (*Clinique médicale*, vol. iii. p. 425, 2d. ed., 1865): "The types seem to depend upon the nature of the miasm, and especially upon the locality which it infects, rather than upon conditions relative to the individual who is affected. Tours and Saumur, both situated on the left bank of the Loire, appear to me to present the same climatic and telluric conditions, yet one observes at Tours only tertian fevers, while the several cases of quartan fever which I have met with there were individuals coming either from Saumur or Rochefort or from other regions where they had contracted it. One of the examples which has most impressed me in connection with the subject is the following: Fourteen soldiers imprisoned at Saumur came to Tours to testify before a court-martial. They had been scarcely ten days in the last town when nine of them were compelled to enter the hospital, affected with quartan fever, the germ of which they had evidently contracted at Saumur, since all the fevers which we observed with the inhabitants of Tours and the neighborhood were of the tertian type."

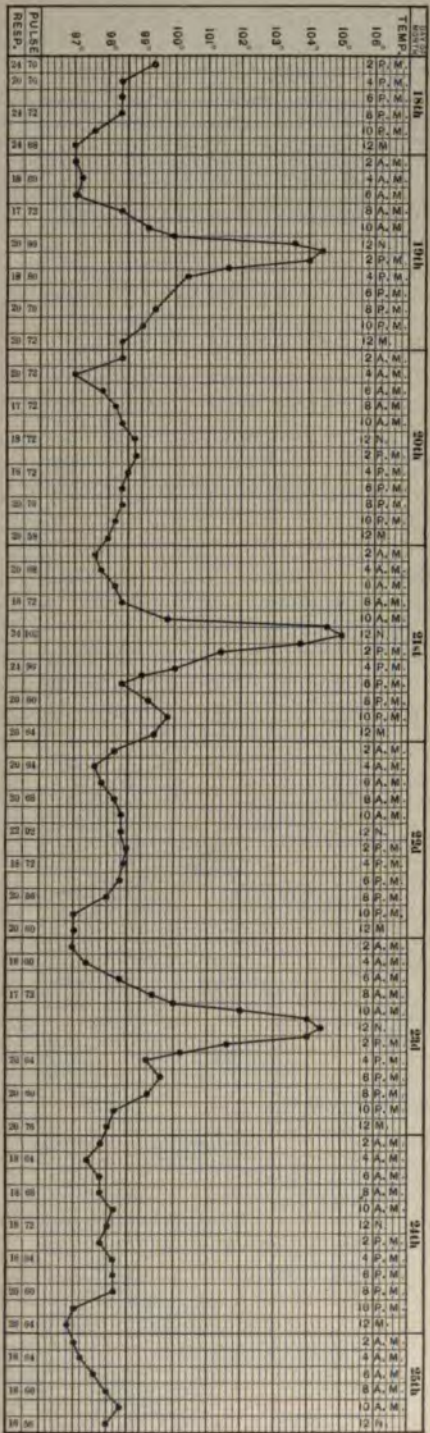
through their cycle of existence together, all the organisms composing the group undergoing segmentation within a period of several hours; it requires, as has been said, approximately forty-eight hours to complete its cycle of development. In infections, then, with a single group of parasites segmentation occurs at intervals approximately forty-eight hours apart. As Golgi so clearly showed, the febrile paroxysm is always associated with the segmentation of a group of malarial parasites, and, as one might expect, the chief characteristic of this type of fever consists in intermittent febrile paroxysms occurring every other day. The regularity with which these paroxysms recur is truly remarkable, the onset sometimes taking place at almost exactly the same hour day after day. More frequently there are slight differences, generally, however, of not more than two hours, between the time at which succeeding paroxysms recur. Our observations of nearly a thousand cases would lead us to believe that slight anticipation in the hour of onset is more common than retardation.

The Paroxysm.—The paroxysm is usually divided into three classical stages: (*a*) the *chill;* (*b*) the *fever;* (*c*) the defervescence or *sweating* stage.

(*a*) *The Chill.*—This may begin without any premonitory symptoms. More commonly, however, for a period of from a few minutes to half an hour the patient complains of uneasy sensations, a slight headache, or perhaps a little giddiness or fatigue. Not infrequently the onset is preceded by yawning. If the temperature is carefully noted during this period, it will usually be found that a slight elevation has already begun to appear. Immediately after this the patient begins to complain of chilly sensations, usually up and down the back; these increase, the patient begins to shiver, and soon a general shaking chill follows. The chill is often extremely violent: the teeth chatter; the whole body is thrown into so violent a tremor that the bed and often surrounding objects in the room are shaken. The skin is pale or often somewhat cyanotic and cool, though wholly disproportionately so in comparison to the intense feeling of cold complained of by the patient. It is often moist, while the erection of the hair follicles gives rise to the characteristic "goose flesh." The pupils are usually dilated. The patient complains often of headache, buzzing in the ears, vertigo, and sometimes of troubles of vision. The pulse is small and rapid and often of rather high tension. There may be nausea and vomiting. The duration of the chill varies materially in different cases; it may last as long as an hour, though usually the period is considerably shorter —from ten minutes to half an hour. Not infrequently no actual shaking occurs, the patient complaining only of chilly sensations. Occasionally, though very rarely in this type of fever, the chill may be entirely absent. Thus out of 339 cases classified by Hewetson and the author at the Johns Hopkins Hospital, chills or chilly sensations were present in 95.5 per cent. of the cases. During the period of the chill the temperature of the patient rises rapidly, and at the end of the chilly sensations may have reached almost its height. Generally, almost the maximum point of temperature is reached within two hours after the onset of the paroxysm.

(*b*) *The Febrile Stage.*—After a certain length of time the chilly sensations become less marked and are interrupted by flushes of heat, which become more frequent, and finally wholly replace the chill. Then begins the second or febrile stage of the paroxysm. The patient complains of an intense burning heat; the skin is flushed, hot, and dry, the conjunctivæ injected, the pulse becomes fuller, but remains rapid; it may be dicrotic. The patient complains bitterly of headache and often of vertigo and buzzing in the ears. The coverings for which but a short time ago he had begged are now thrown aside. Often there is intense thirst. The patient is frequently restless, throwing himself from one side of the bed to the other. In some instances there is active delirium. A case observed by the author jumped from the window of the ward during the febrile stage of a double tertian paroxysm, killing himself by the fall. In other instances the patient is dull, drowsy, and typhoidal in appearance, complaining upon inquiry only of intense headache and aching pains in the back and the extremities. Not infrequently there is a slight cough. Sometimes there is vomiting or diarrhœa. Bleeding from the nose occasionally occurs.

On physical examination the face is flushed, the conjunctivæ are injected; the tongue is often dry and coated. There is often a dusky, yellowish-gray color



Tertian intermittent fever.

FIG. 1.

to the skin, while the lips and mucous membranes are pale. Herpes on the lips and nose is very common. Various cutaneous eruptions have been noted, usually erythematous in nature. In several instances the author has observed an extensive general urticaria. The respiration is not particularly accelerated, though the pulse is often rapid and sometimes dicrotic. The lungs are generally clear on auscultation and percussion, though, not infrequently, evidences of a general bronchitis—sonorous and sibillant râles—may be heard throughout the chest, more frequently in the back. The heart sounds are usually clear, though a soft systolic murmur may be heard over the body of the heart. The abdomen is generally natural in appearance. The area of hepatic dulness is often somewhat increased. There is frequently tenderness on pressure in the region of the spleen, while the area of the splenic dulness is almost invariably increased. In most cases the spleen is easily palpable. This has been the case in 73.4 per cent. of our cases in which notes were made. In fresh cases the border is rounded and soft; in older cases, where there have been numerous previous attacks, the border is often sharp and firm, reaching sometimes a considerable distance below the costal margin. The splenic tumor is particularly striking in children. The most marked splenic enlargements occur, however, in the more irregular æstivo-autumnal fevers. Massuriany[1] noted the presence of a soft souffle over the splenic area, which Bouchard has compared to the uterine bruit. During this period the temperature reaches its maximum point. Temperatures as high as 108° F. have been noted. The duration of the febrile period is usually four or five hours, though, not infrequently, considerably longer.

(c) *The Sweating Stage.*—After the stage of fever has existed for four or five hours it is usually followed quite suddenly by the third or sweating stage of the paroxysm. The patient begins to feel relief from the sensation of oppressive heat from which he has been suffering, and then, quite suddenly, breaks into a profuse sweat. The sweating is often excessive; the night-clothes and bedding may be soaked. In association with this the temperature falls, usually quite rapidly. The pulse, which has been rapid, becomes slow and full, and the patient often passes into a refreshing sleep. The temperature falls, almost invariably to a subnormal point. The duration of the sweating stage varies considerably. The defervescence is generally somewhat longer than the rise of temperature, though it may be very short and sudden; it commonly lasts from two to four hours, though often somewhat longer.

The average length of the entire paroxysm from the time the temperature passed 99° F. until it reached this point again averaged, in 173 cases observed by the author, about eleven hours. The paroxysms occur more frequently during the day than during the night, the onset being, perhaps, more commonly noted between midnight and noon, though it may occur at any hour of the day or night; indeed, paroxysms beginning in the afternoon are not at all uncommon.

In *children* the paroxysm differs often from that observed in adults. Very commonly in young children both the first and third stages, the chill and the sweating, may be absent or abortive. The first stage is then generally represented by a slight restlessness. The face looks pinched, the eyes are sunken; the finger-tips and toes become cyanotic and cold, while the child may yawn and stretch itself. Nausea, vomiting and diarrhœa are particularly common. These may be the only manifestations of the first stage. Commonly, however, these symptoms are followed by grave nervous phenomena. The chill in malaria, as in other acute diseases, is not infrequently represented in the young child by general convulsions. These begin usually with a slight spasmodic twitching of the eyelids or of the extremities, the spasm soon becoming general. The febrile stage and the whole paroxysm are often shorter in the child than in the adult. The sweating stage may be wholly absent. In many instances, besides a slight coldness of the hands and blueness of the finger-tips, and a somewhat pinched expression of the face in the first stage, the first and third stage of the paroxysm may be entirely lacking.

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[1] *St. Pet. med. Woch.*, 1884.

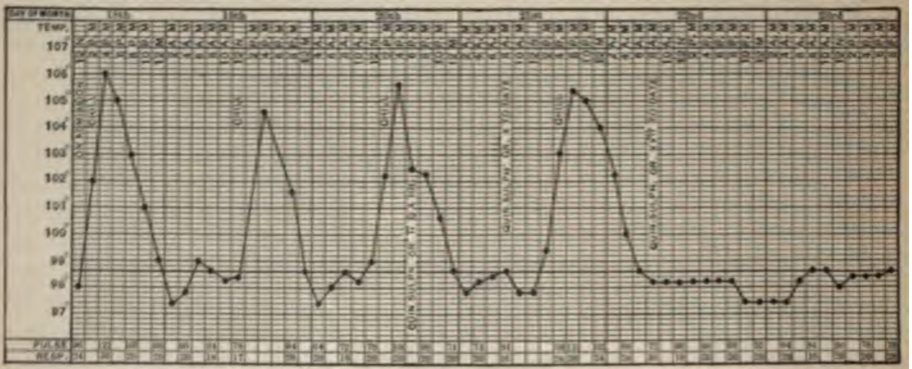
The Intermission.—In the period of intermission the patient often feels quite well, so much so that it is not uncommon for patients to pass through a number of paroxysms before consulting a physician, believing after each that the disease is at an end. The temperature after the sweating stage becomes almost invariably subnormal, and often remains so during the greater part of the next day. About forty-eight hours after the onset of the first paroxysm the fresh group of parasites proceeding from the segmentation of two days before having reached maturity and entered again upon segmentation, a fresh paroxysm begins. Often, as has been said, the time of onset of several successive paroxysms is almost exactly the same. More commonly, though, there are slight variations of an hour or two, anticipation or retardation. In these instances the parasite passes through its cycle of existence a little quicker or a little slower than in the typical forty-eight hours. Slightly anticipating paroxysms are very common, more so than retardation.

The Blood.—The blood shows the presence of one group of the characteristic tertian parasites. These organisms are to be followed through all the stages of their development. They are most striking and most readily observed several hours before the paroxysm, when they are large and contain most pigment. At the time of the paroxysm and immediately before this the picture may not be so striking, as many of the parasites which, earlier in development, are to be found with great frequency in the general peripheral circulation, become accumulated in certain of the internal organs, where they remain during the period of segmentation. Segmenting parasites are usually to be found in the peripheral circulation, the first being seen several hours before the onset of the paroxysm; at times they may be present in large numbers. Large swollen forms of the organism with very active pigment granules, or deformed and vacuolated forms, are also common during this period. Often the fragmentation of these bodies may be seen, and numerous small pigmented extracellular forms resulting from this fragmentation may be found. These swollen vacuolated and fragmented forms appear to be more common where recovery is taking place, and there is every reason to believe that they represent full-grown parasites which, failing to undergo segmentation, have become degenerate and sterile. During and just after the paroxysm the process of phagocytosis may often be observed under the microscope, and pigmented leucocytes are always present. The elements taken up are for the most part the free pigment clumps from segmenting forms, the segmenting form itself, fragmented extracellular bodies, and flagellate forms.

(2) *Double Infections.—Quotidian Intermittent Fever.*—Single tertian infections are among the mildest forms of malarial fever which are observed in temperate climates; more commonly the individual shows an infection with two groups of the tertian parasite. These groups reach maturity on alternate days. Segmentation, then, of a group of parasites occurs every day, and, as one might expect, daily paroxysms, *quotidian intermittent fever*, result. The paroxysms in these instances are similar in every way to those of single tertian infections. The manner of onset and duration are the same, while during the periods of intermission the temperature is likewise almost always subnormal. It is common, however, for the paroxysms on successive days to show slight constant differences in their hours of onset, one group of parasites arriving at maturity at an hour slightly different from that of the other. These differences are usually not great, though they may be considerable, one paroxysm beginning in the morning, that upon the following day in the afternoon. Very commonly one set of organisms is more numerous than the other, causing thus a more severe paroxysm. The chart then shows alternate mild and severe attacks. These facts alone might lead us to recognize the dependence of this quotidian fever upon a double infection without the confirmation obtained by examination of the blood.

The *blood* shows the presence of two groups of the tertian parasite in different stages of development. Thus at the time of the paroxysm, while one group is full grown and in the stage of segmentation, the other is represented by smaller, slightly pigmented, actively amœboid bodies. The question of the origin of these double tertian infections is interesting and by no means wholly clear. Very commonly the first several paroxysms are tertian in nature, daily chills appearing only later on in the course. This may well be, and probably is due to the fact that at the time of the original infection there were two groups of

FIG. 2.



Double tertian infection (quotidian fever).

parasites, one of which was so much smaller than the other as to take materially longer to reach a size sufficient to produce a paroxysm. On the other hand, some observers have suggested that the origin of double infections may be due to the lagging behind of certain parasites out of an originally single group, these retarded forms eventually forming a group of their own. If this be the case, however, it is remarkable that the retardation should be almost exactly twenty-four hours behind that of the original group. Indeed, the remarkable similarity in the hours of the paroxysms due to two different groups of the parasite is striking and not easily explained.

Infections with multiple groups of parasites have been described. These result, naturally, in more irregular subcontinuous fever. This is, however, extremely rare. Only one doubtful case of this nature has been observed by the author. The examination of the blood in these instances shows organisms in all stages of development; there is great difficulty here in distinguishing separate groups.

QUARTAN FEVER.—(1) *Single Infections.—Quartan Intermittent Fever;* (2) *Double Infections.—Double Quartan Intermittent Fever;* (3) *Triple Infections.—Quotidian (Triple Quartan) Intermittent Fever.*

(1) *Single Infections.—Quartan Intermittent Fever.*—This type of fever depends upon the presence in the blood of the quartan parasite, an organism which, just as in the case of the tertian parasite, possesses the remarkable characteristic of existing in the blood in great groups, all the members of which are, approximately, at the same stage of development. The cycle of development of the quartan parasite lasts approximately seventy-two hours, segmentation occurring every fourth day. The characteristics, then, of single quartan infections are quartan intermittent paroxysms, two days of complete intermission existing between. The paroxysm in quartan fever resembles in all its features that observed in tertian infection. The duration in the cases seen by the author averaged between ten and eleven hours. The same periods of subnormal temperature, lasting often during the greater part of the two days of intermission, are observed. The regularity of the paroxysms in quartan infection is the most remarkable characteristic of the disease. A tendency toward anticipation or retardation in the paroxysms is less often noted than in tertian infection.

The blood shows the presence of a quartan parasite. The development of the organism may be readily followed. It is most clearly demonstrated just before and during the paroxysm when the parasites are full grown. The tendency of the full grown and sporulating forms to accumulate in the internal organs—a tendency which has been noted in tertian fever, and exists, as will be stated later, to a greater extent in æstivo-autumnal fever—is not to be observed in the case of the quartan organism; all stages of development may be seen with equal frequency in the peripheral circulation. At the time when the parasite reaches maturity swollen, fragmented, and vacuolated forms may be seen as in tertian fever. They are, however, less frequent, as are also the flagellate bodies.

(2) *Double Infections.—Double Quartan Fever.*—Often more than one group of quartan parasites may be present in the blood at the same time. When two groups are present segmentation usually occurs on two suc-

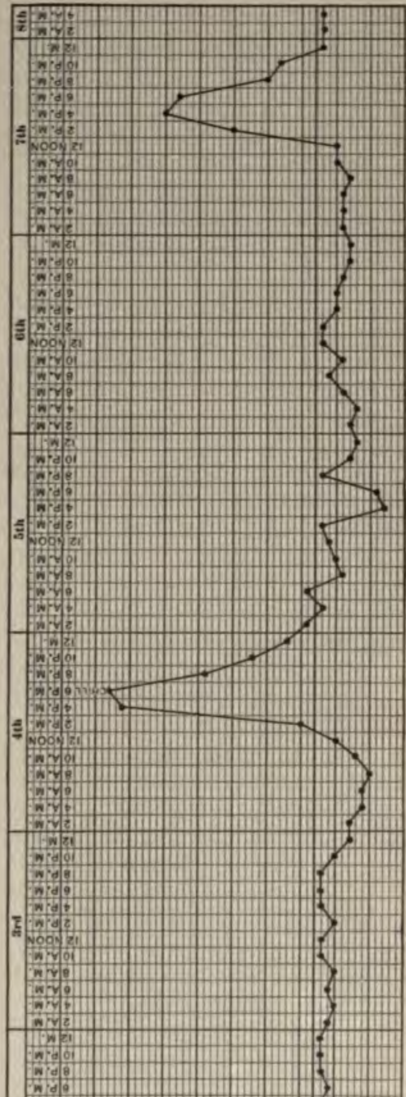


FIG. 3.

Quartan Intermittent fever.

cessive days, with a day of intermission following. Clinically, therefore, these double infections are characterized by chills upon two successive days, with a day of complete intermission following. The paroxysms in these instances are exactly similar to those observed in single infection. The examination of the blood, however, shows the presence of two groups of the quartan parasite.

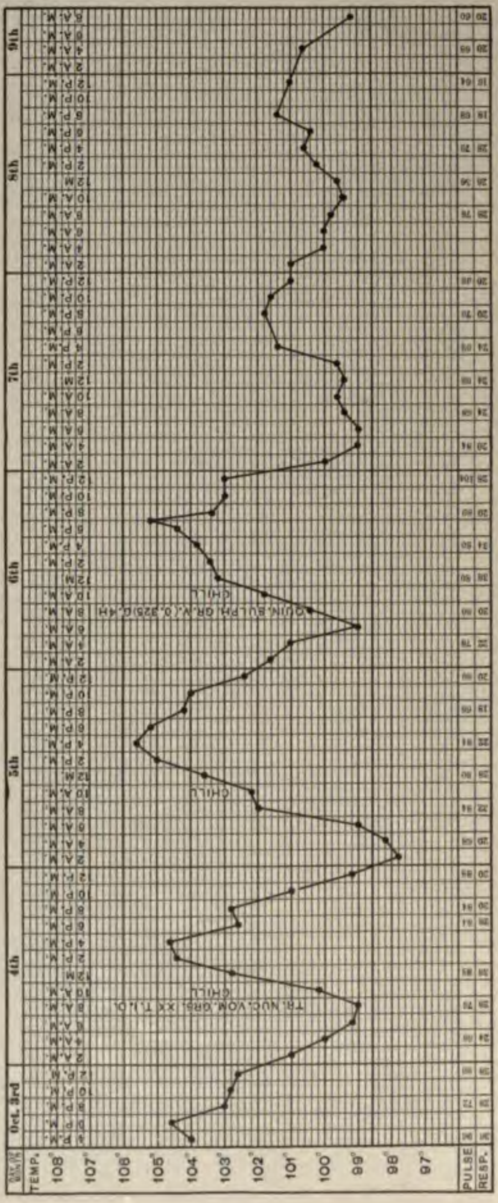
(3) *Triple Infections.—Triple Quartan Fever.*—Very commonly three groups of the quartan parasite may be present in the blood at the same time. These groups reach maturity on successive days, and cause, therefore, quotidian intermittent fever. The symptoms of quotidian fever depending upon a triple quartan infection differ often in no wise from those depending upon a double tertian infection. Daily paroxysms, exactly similar in nature, occur in both instances. The same period of subnormal temperature may be noted, and the diagnosis, without the examination of the blood, may be impossible. Examination of the blood in these instances shows, however, the presence of three groups of the quartan parasite, each in different stages of development.

ÆSTIVO-AUTUMNAL FEVER.—This type of fever differs materially from the regularly intermittent fevers of the early part of the malarial season. It depends upon the presence in the blood of the smaller organism first described by Marchiafava and Celli, the æstivo-autumnal parasite. This parasite, as has been previously stated, possesses to a much less marked degree the characteristic of existing in large sharply defined groups, while, as has also been noted, the length of the cycle of existence appears to vary considerably. At the beginning of many infections an arrangement in groups may, however, be made out, and this arrangement may exist for a certain length of time. Usually, however, before the process has lasted very long organisms in different stages of development may be found at any time during the fever. In some instances groups of parasites with a cycle lasting about twenty-four hours have apparently been made out, while in others fairly distinct groups appear to pass through a cycle lasting considerably longer, as long as forty-eight hours or even more. Clinically, æstivo-autumnal fever appears in very varied forms.

Not infrequently it may be seen in the form of *quotidian intermittent fever*. Here the paroxysms may resemble very closely those of tertian or quartan fever, and in some instances, without the examination of the blood, the distinction from double tertian or triple quartan infections cannot be made. In these instances the process begins with a sharp chill and ends with a well marked sweating stage, the duration of the paroxysm being perhaps exactly similar to that in the regularly intermittent fevers. More commonly, however, the paroxysms are longer and more drawn out, lasting perhaps as long as twenty hours. Here the first stage often differs greatly from that in tertian or quartan fever. While in the regularly intermittent fevers the onset is rapid and usually associated with a chill, in these instances the rise may be much more gradual, while the chill is not infrequently altogether lacking. Often a slight transient chill may be observed some time after the beginning of the rise in temperature. The chill in æstivo-autumnal fever can by no means be called the *initial* symptom in the paroxysm; the fever has often become well marked before the onset of the rigor. Usually, after a certain number of paroxysms, a distinct irregularity in the fever becomes evident. Either from the lengthening out of one of the paroxysms or from the anticipation of the following paroxysm the intermission between the two becomes, perhaps, completely obliterated or indicated only by a slight drop in temperature, until finally there results an irregular continued fever in which all trace of the paroxysm has disappeared.

Not infrequently the early paroxysms recur at greater intervals one from the other. These intervals are frequently forty-eight hours, more or less ("*Æstivo-autumnal tertian fever; malignant tertian fever*"—Marchiafava and Bignami). In these instances the paroxysms are usually particularly long, lasting sometimes as much as thirty-six hours. The very gradual rise in temperature, which is often unaccompanied by a chill, and the slow fall, are in striking contrast to the chart of an ordinary tertian fever. Marchiafava and Bignami, who, as has been before stated, believe that they can distinguish two separate types of the æstivo-autumnal parasite, the quotidian and the tertian, have described minutely the fever curve in these cases with longer intervals. This class of cases they term "*malignant tertian fever*," in contradistinction to the milder regularly intermittent tertian fever. They describe what they believe to be a characteristic fever curve, the more or less sudden onset of the symptoms, a pseudo-crisis, a precritical elevation of temperature, which often reaches a point higher than has been viously attained, and, finally, the actual crisis. Charts similar to

FIG. 4.



Æstivo-autumnal fever (quotidian paroxysms).

have been observed by the author and reproduced in a recent pub tion (see Fig. 5), though he has not seen a sufficient number o stances to justify him in believing that such a curve is characte of a particular, separate type of parasite. It is certainly true, how that irregular oscillations in the curve of the fever produced by these parasites are very common. The periods of intermission between par-

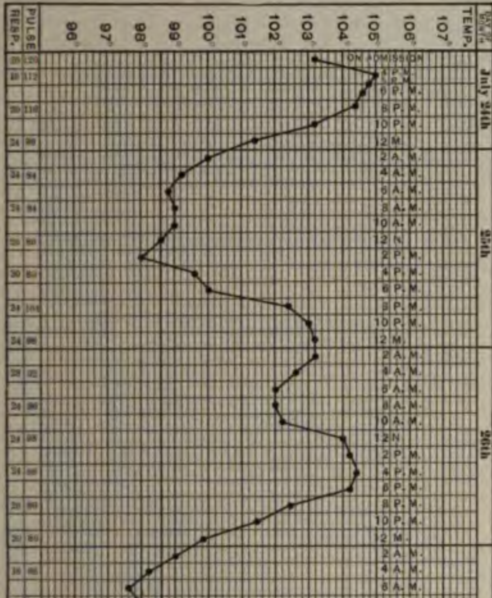


Fig. 5.

Æstivo-autumnal fever (paroxysms at intervals of forty-eight hours).

ysms show, usually, a subnormal temperature. The periods of apy-
xia are, however, very brief, as one may readily conceive when he
siders the length of the paroxysm, lasting, as it often does, thirty-six
urs or over.

In those cases in which the paroxysms occur at intervals of approximately forty-eight hours, one from another, the irregularity in the hour of onset of the paroxysms is particularly striking. In some cases there is marked retardation, intervals of considerably more than forty-eight hours occurring between the beginning of one paroxysm and that of its successor. More frequently, however, there is anticipation, the paroxysms recurring at intervals of less than forty-eight hours. Now, if, as already stated, the individual paroxysm should last thirty-six hours or more, it may be readily seen how short the period of intermission in these cases would be. Often, then, there is an almost continuous high temperature, with occasional remissions or intermissions lasting, perhaps, less than an hour—"*malarial remittent fever.*"

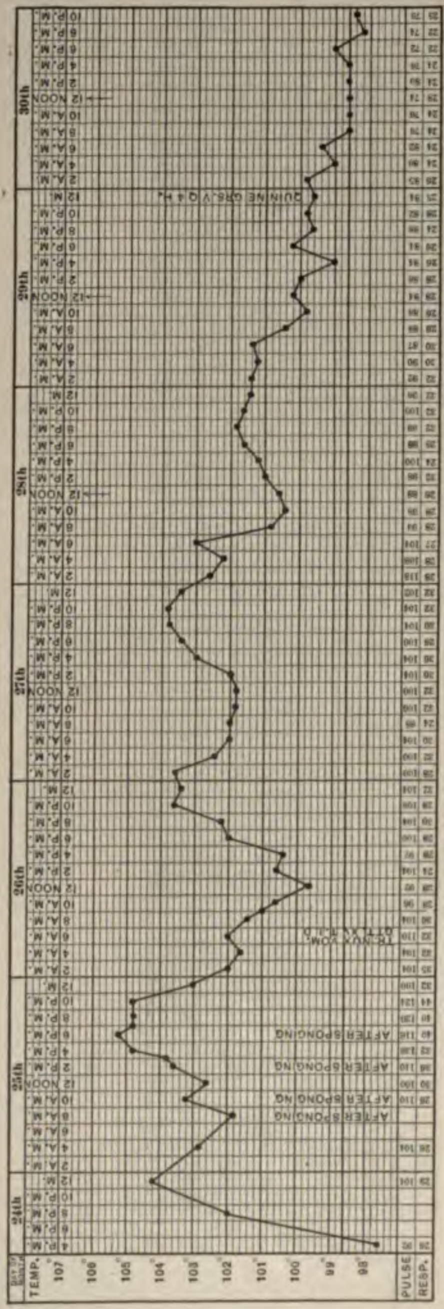


FIG. 6.

Æstivo-autumnal fever (showing the development of remittent and continued fevers).

In many instances the new paroxysm begins before the previous one has finished, owing either to an excessive prolongation of the first paroxysm or to an anticipation of the succeeding one. In these cases the result is, of course, a *continuous* fever. Usually, the continuous fevers resulting from æstivo-autumnal infections, though the temperature may never reach the normal point, yet show indications of the paroxysms and sometimes occasional abortive chills. In some instances, however, all evidence of paroxysms may be absent, the chart closely simulating that of typhoid fever. Such cases are probably often due to infections with more than one group of parasites. It is probably true that the long duration of some of the paroxysms is accounted for by the fact that the segmentation of a given group of parasites occurs through an appreciably greater length of time than in the regularly intermittent fevers.

The result of all this is that the chart of æstivo-autumnal fever presents very commonly somewhat the following picture: At the onset there are several intermittent paroxysms occurring at intervals of from twenty-four to forty-eight hours or a little more. After a few of these attacks the fever becomes irregular or continued. This may occur, as has been said, in several ways: (1) *Through modifications of the curve in the individual paroxysm;* (2) *by modification in succession of the paroxysms.*

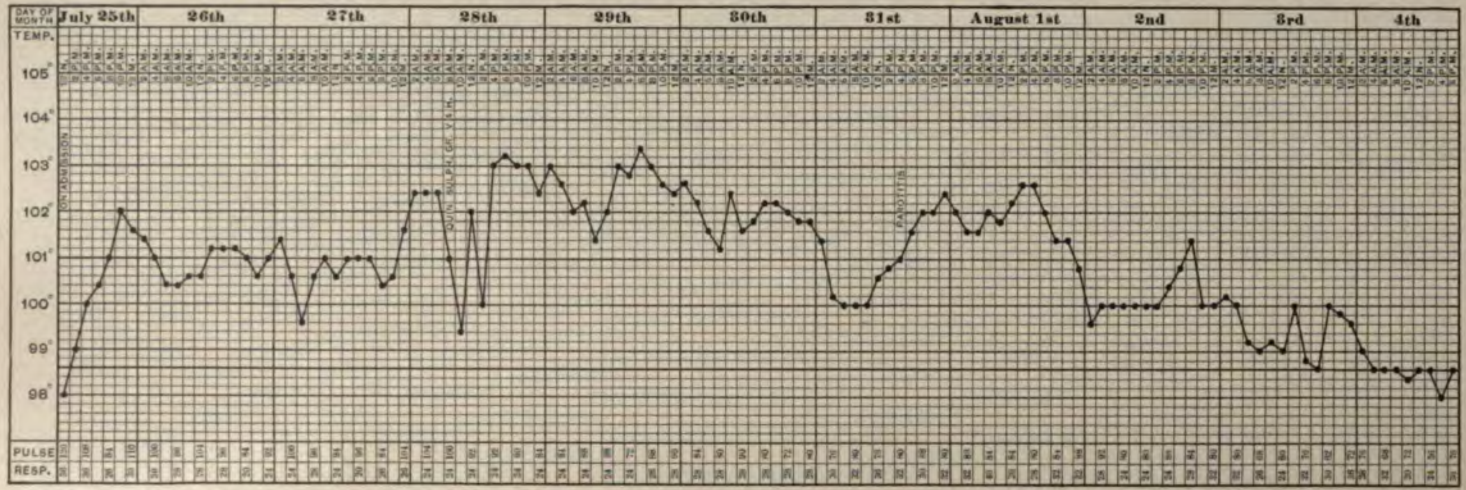
(1) *The important modifications of the curve* are the following: (*a*) The lack of a sharp initial elevation, so that the curve rises in a slow and continuous manner; (*b*) the occurrence of a pseudo-crisis, so that the attack tends to lose its individuality; (*c*) the prolongation of the paroxysm, which is usually associated with an exaggeration of the thermic oscillations during the fastigium.

(2) *The modifications in the succession of the paroxysms may be* (*a*) the anticipation of the paroxysms; (*b*) the retardation of the paroxysms; (*c*) the prolongation of the paroxysms, by which apyrexia is made incomplete; (*d*) the occurrence of slight oscillations in temperature during the period which ought to be one of apyrexia; (*e*) the reduplication of the attack.

Very often when the case first comes under observation it is already one of "remittent" or continued fever. The chills are frequently absent; the patient complains bitterly of headache and general pain in his back and extremities. He is usually dull, drowsy, and apathetic, though there may be marked delirium. The face is flushed, the conjunctivæ are injected, the tongue dry and coated; there is sordes upon the lips and teeth; the patient remains continuously in a condition similar to that described in the febrile stage of the ordinary paroxysm. In these instances it is often absolutely impossible, without examination of the blood, to distinguish the case from one of typhoid fever. The writer has repeatedly seen patients with æstivo-autumnal malaria placed under treatment as cases of typhoid fever, the attention being first drawn to the true condition of things by a sudden fall of the temperature to normal, or by the discovery of the small amœboid hyaline parasites within the red corpuscles. Grave cerebral or abdominal symptoms develop, often early in the course of these subcontinuous fevers, which frequently tend to become pernicious. Careful observations may show that these symptoms are paroxysmal. Delirium, drowsiness, stupor, coma, grave cerebral symptoms, local spasms, general convulsive seizures may occur, or perhaps profuse vomiting or a choleriform diarrhœa with collapse. In fact, any of the symptoms which will be discussed under the Pernicious Fevers may suddenly develop in the course of subcontinuous æstivo-autumnal infection.

These instances of more or less continued fever are occasionally referred to as "*malarial remittent fever.*" They have been admirably described by Baccelli, who recognized their true malarial nature, under

Fig. 7.



Æstivo-autumnal fever; continued fever; "subcontinua typhoidea." (The fever after the 31st was due to an acute parotitis.)

the name of "*subcontinua typhoidea.*" As has been previously stated, the tendency of the regularly intermittent fevers, when left to themselves, is toward spontaneous recovery after a certain number of paroxysms, and, while relapses are common and productive, perhaps, of grave secondary disturbances—anæmia, nephritis, etc.—the tendency to become pernicious is rarely observed. This is not true of æstivo-autumnal infections as a class. In many instances, to be sure, when placed under hygienic conditions the same tendency toward spontaneous recovery, usually with relapses, is to be observed. Often, however, an untreated infection becomes steadily more aggravated, until, finally, so-called "pernicious" symptoms appear and a fatal result ensues.

In other instances an æstivo-autumnal infection may be associated with but *slight irregular rises in temperature;* there may be no sharp paroxysms, the patient complaining only of languor, anorexia, headache, pains in the back and limbs. Such instances may easily lead to errors in diagnosis. There is usually, if the case has existed for any length of time, a certain degree of anæmia, with the characteristic sallow hue to the skin, while the spleen is almost always enlarged. Such cases probably often pass into the condition which will be later described as "chronic malarial cachexia."

PERNICIOUS MALARIAL FEVERS.—These very malignant forms of malarial fever have, in this and other languages, generally acquired the name "*the pernicious fevers.*" It is quite true that the term "malignant fevers" used by the translators of Marchiafava and Bignami's[1] work is, in the abstract, better, but the word "pernicious" is so firmly implanted in the general usage that its eradication appears to the writer injudicious.

Pernicious fever depends, almost invariably, upon infection with the æstivo-autumnal parasite. In temperate climates these fevers are rare, but in the tropics they are extremely common. The pernicious nature of an attack depends, generally, as has been shown in the section on *Pathological Anatomy* (page 83), upon several causes: (1) The great numbers of parasites present and their capacity for rapid multiplication; (2) the special involvement of certain vital organs by the parasites, which, as has been pointed out, show a remarkable tendency toward accumulation in certain definite organs, varying in different cases; (3) possibly upon the greater or less virulence of the parasite. This latter statement is based upon the assumption that the malarial parasites produce a specific toxic substance. Certain authors thus believe that, in the case of infection with a very malignant parasite, pernicious symptoms may result, while but a small number of parasites are present, particularly if the chief seat of development of the parasite be localized in a particularly vital spot. This is, however, doubtful. While it is probable that a specific toxic substance may be produced by the parasite, and while there is very good reason to believe that there is a difference between the malignity of the parasites in different instances, yet, in a general way, the severity of the symptoms, as demonstrated long ago by Golgi, appears to depend largely upon the number of parasites present. And in a general way it may be definitely stated that pernicious fever never occurs without the presence of a considerable number of parasites, though in some of these instances very few organisms may be found in the peripheral circulation.

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[1] *The Parasites of Malarial Fevers*, New Sydenham Society, 1894.

Bastianelli and Bignàmi in a recent article[1] well say: "The conditions through which a malarial infection becomes pernicious are: (1) That the infection be produced by one of the varieties of the æstivo-autumnal parasite. On this condition all today are agreed, and we shall not insist further.[2] (2) The second condition relates to the abundance of the parasites, and it may be stated as follows: In pernicious fevers, if one takes into consideration not only the examination of the blood from the finger, but also the condition in the vessels of the various organs (Marchiafava, Celli, Bignami), it is a striking point that, however the distribution of the parasites may vary in individual cases, their total number is always considerable. As regards the distribution, one may make the following distinctions: There exist (1) cases in which the number of parasites is most abundant, yes enormous, while all the organs are uniformly invaded. These are the most common forms of pernicious fever, and are usually accompanied by coma. There are some cases in this category in which the number of parasites in the blood of the finger, of the spleen, of the bone marrow, etc. is enormous, while the number in the brain is scanty; clinically, the absence of cerebral phenomena is noted. (2) Cases in which the number of parasites is absolutely and relatively scanty in the bone marrow, in the spleen, in the liver, while there may be relatively few in the blood of the finger, yet other organs are crowded with parasites. Among these the following localizations are to be made out: (*a*) The brain and the meninges are filled with parasites either in sporulation or in all their stages of development; in such cases it is difficult to find not only sporulating forms, but even young parasites in the spleen. Clinically, there are cerebral phenomena. (*b*) The stomach and intestine are chiefly invaded; in these organs the mature forms of the parasite are usually found; these are the cases of pernicious fever which present, clinically, ... intestinal phenomena."

The pernicious symptoms may come on quite early in the course of the infection, though usually several paroxysms have existed before their appearance. In very malarious districts, however, almost the first paroxysm observed may be pernicious in nature.

THE COMATOSE TYPE.—The commonest form of pernicious malaria is that accompanied by coma. Here, in the earlier part of the paroxysm, the patient may be slightly delirious, but he soon becomes drowsy and somnolent, passing finally into a condition of profound coma. Not infrequently, in grave malarious districts, the patient comes for the first time to the observation of the physician while in this condition. He is profoundly unconscious; the respiration is often stertorous, and occasionally of the Cheyne-Stokes type. The pupils may be contracted or dilated, sometimes perhaps unequal. There is often—a not unimportant point—a slight jaundice. Not infrequently there is hiccough; the pulse may be full and slow and of high tension, though toward the end it is often rapid, irregular, and feeble. Local spasms of certain muscles may occur. Thus, in one of the author's cases there was a well marked spasm of the lower facial muscles on one side, which disappeared with the paroxysm. Recovery may result after the gravest symptoms, but without treatment the paroxysm is usually followed rapidly by a second, which generally proves fatal.

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[1] *Bull. d. R. Acc. Med. di Roma*, 1893–94, Anno xv., v. xx. 186.

[2] There are exceptions, though rare, to this rule. Dr. Walter Reed of the Army Medical Museum in Washington has recently communicated to me his observation of specimens from a case of characteristic comatose pernicious fever due to a double tertian infection. This case has since been reported by Dr. Wm. B. French of Washington (*N. Y. Med. Journal*, 1895, vol. lxiii. p. 674).

OTHER CEREBRAL MANIFESTATIONS.—In other instances most decided cerebral symptoms of a different nature may occur. *Delirium* which may be maniacal may be observed. Active *delusions* and *hallucinations* are not uncommon, while in some instances *tetanic convulsions* have been noted. In a number of instances *hemiplegia* has been associated with the paroxysm, disappearing after the attack. At times distinct symptoms of bulbar paralysis may occur. In one of these cases carefully studied by Marchiafava[1] the special localization of the parasites in certain foci in the medulla was confirmed postmortem.

HEMORRHAGIC TYPE.—In some instances of pernicious fever grave hemorrhagic symptoms may occur—epistaxis, hæmoptysis, extensive cutaneous hemorrhages. Several of these cases are described by Marchiafava and Bignami.[2]

ALGID TYPE.—This is sometimes extremely insidious and fatal. After several paroxysms which are in no way remarkable the patient very suddenly passes into a condition of extreme collapse. This does not occur at the beginning of the paroxysm, but at the time when the stage of fever should exist. The temperature may be but slightly elevated; indeed, in some instances it is subnormal. The condition is not unlike that in Asiatic cholera. The mind is clear, there is little suffering, but extreme collapse. The eyes are sunken; the features drawn and pinched; the face expressionless; the tongue dry; the skin moist and covered with a cold sweat. The patient may be so quiet and uncomplaining that it may be, as Laveran states, only through an accidental examination of the pulse that the true state of affairs may be discovered. The pulse is very rapid and feeble and thready, almost impalpable, becoming imperceptible at the wrist before death. Physical examination of the thorax is negative excepting for the feeble action of the heart. The second sound at the base may be quite inaudible. The abdomen is usually retracted; there is often tenderness on pressure in the region of the spleen, which is palpable.

SUDORIFEROUS TYPE.—A sudoriferous type of paroxysm has been described, in which, during the last stage, the sweating becomes excessive and the patient passes into a condition of collapse with a thready pulse and cold extremities. Without vigorous interference the case may end fatally.

BILIOUS TYPE.—A type of paroxysm has been described by certain observers, the chief symptom of which is the vomiting of large quantities of bile-stained fluid; this is usually associated with stools of a similar nature.

GASTRALGIC AND CARDIALGIC TYPES.—Severe gastralgic paroxysms associated with profuse vomiting, and often with hæmatemesis, may occur without the existence of striking intestinal symptoms. An attack of this nature is well described by Laveran.[1]

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[1] *Lav. d. III. Cong. d. soc. It. d. Med. Int.*, Roma, 1890, 142.

[2] *Loc. cit.*

CHOLERIFORM TYPE.—In certain instances in which the chief localization of the parasite is in the stomach and intestines the patients present a clinical picture strongly resembling that of Asiatic cholera. These cases have been particularly studied by Marchiafava.[2] The paroxysm usually begins with profuse vomiting and diarrhœa; the discharges may resemble those of cholera. The skin is cold, moist, and clammy. There is cyanosis of the lips and extremities; the pulse is rapid and thread-like. There may be cramps in the extremities. The condition closely resembles the algid stage of Asiatic cholera. If the paroxysm be not fatal, profuse sweating may follow, with an intermission in the symptoms. Anatomically, the mucous membrane of the stomach and intestines is found to be filled with malarial parasites. These may produce actual thrombosis of the vessels of the mucous membrane with superficial necroses and ulceration.

PNEUMONIC OR DYSPNŒIC TYPE.—Baccelli[3] and others have described a type of paroxysm the symptoms of which suggest strongly a pneumonia. This admirable observer, however, as long ago as 1866 recognized this condition to be distinct from a true complicating pneumonia. There is intense thoracic pain, great dyspnœa, and a painful cough. There may be moderate dulness over the affected lung with coarse, sonorous, and sibilant and finer moist râles. Laveran[4] has seen a fairly abundant hæmoptysis following an acute dyspnœic paroxysm. In other instances, despite the extreme dyspnœa, physical examination may be quite negative. The sputum is mixed with dark fluid and clotted blood. The condition is certainly not a pneumonia; it is more probably an active congestion of the pulmonary vessels. In the absence of autopsy records in cases of this nature one can but suspect that they represent a special localization of the parasite in the pulmonary capillaries.

HÆMOGLOBINURIC TYPE—"*Malarial hæmaturia.*"—Hæmoglobinuria is a not uncommon symptom in the graver fevers in certain malarious districts. In temperate climates it is rarely seen. The ultimate cause of its production is not yet settled. A continual destruction of the red blood-corpuscles is going on throughout every malarial infection. This occurs in various ways: (1) The parasites, developing within the corpuscles, form the black pigment, melanin, at the expense of the corpuscles in which they grow, the corpuscles becoming gradually decolorized and destroyed. (2) In many instances the red blood-corpuscles containing the parasite undergo a premature necrosis, becoming brassy colored and shrunken. (3) Sometimes the decolorization of the corpuscles containing the parasite occurs quite suddenly, the corpuscles bursting, as it were, and setting free their hæmoglobin in the blood current. Thus, during an ordinary malarial attack there is always a certain amount of hæmoglobin set free in the serum, but, as this amount does not pass beyond the limit of the quantity which can be disposed of by the liver, it does not appear in the urine.

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[1] *Traité des Fièvres palustres*, Obs. xxxviii.

[2] *Cent. f. Allg. Path. u. Path. Anat.*, 1894, V. No. 10, 418.

[3] *Studien über Malaria*, Berlin, 1895.

[4] *Traité des Fièvres palustres.*

It is doubtless, in part, to this constant destruction of the red corpuscles, with the liberation of their hæmoglobin, that the polycholia and slight jaundice so commonly observed in malaria are due. Ponfick estimates that up to one sixth the total number of the red blood-corpuscles may be destroyed and disposed of in the economy without the hæmoglobin appearing, as such, in the urine. If this destruction of the red blood-corpuscles becomes unusually great, and the quantity of hæmoglobin separated from the disco-plasma of the red blood-corpuscles exceeds the amount which can be taken care of by the liver, hæmoglobinuria will result. It is not, however, only the infected corpuscles which lose their hæmoglobin in these instances; great numbers of their uninfected fellows are equally affected, just as in the ordinary paroxysmal hæmoglobinuria. Some substance excessively toxic to the disco-plasma of the red blood-corpuscles must be present in the circulation, or some change has taken place in the blood serum by which it has lost its isotonicity, but what these changes are and to what they are due are by no means clear. There is much which might lead us to believe with Baccelli that some toxic substance, produced perhaps by the parasite itself, may be at the bottom of these changes. Why, however, hæmoglobinuria should be so common in certain regions—as, for instance, Greece and West Africa—and so infrequent in many other more malarious districts is quite inexplicable in the present state of our knowledge.

Clinically, these cases are among the severest forms of malarial fever. The same condition is known in Western Africa as "*black water fever*." By many observers, particularly by the French, the term *bilious hæmoglobinuric fever* has been used. Not infrequently the term "*hæmaturic*" is used, and, indeed, as the interesting researches of Joseph Jones show, actual hæmaturia often occurs. The hæmoglobinuric attack is rarely the initial symptom of the infection. Usually the patient has had repeated attacks of malaria, the hæmoglobinuria appearing suddenly with a relapse, or, if it be the first infection, the hæmoglobinuric attack is preceded by several intermittent paroxysms. In cases where either in a relapse or in a primary infection the hæmoglobinuria appears with the first actual paroxysm, there are often prodromal symptoms lasting for from several hours to sometimes several days. It is probable that these are associated with moderate fever and often represent abortive paroxysms. There are loss of appetite, headache, indefinite pains in the extremities and back. It may be remembered that in many paroxysms of the more ordinary types of æstivo-autumnal fever the gradual onset of the paroxysm without chill is frequent: this is not true in the case of the hæmoglobinuric paroxysm, which begins almost invariably with a severe shaking chill. This is followed by intense pain in the back, head, and extremities, and by profuse vomiting; the vomitus consists of a deeply bile-stained fluid. The face is flushed; the conjunctivæ are injected; the pulse is rapid; the patient is usually in a condition of great anxiety and apprehension. There is a well marked icteric hue to the skin. There is usually profuse diarrhœa.

The first *urine* that is passed, in the early stage of the paroxysm, has a somewhat rosy reddish hue. This, however, rapidly becomes deeper, and is finally an intense brownish black color with something of a greenish tinge, and a greenish yellow foam on shaking. The vomitus becomes of a deeper color, at first yellow, then green, finally sometimes almost black. There may be diarrhœa, the dejecta being green or brown in color, while in other instances there is constipation. During the stage of fever the patient generally becomes jaundiced. There is usually little delirium, the patient being quite conscious and in a condition of great anxiety and agitation. He often complains of severe epigastric pain, which is possibly associated with repeated vomiting; in other instances the pains in the loins may be extremely severe, bearing, possibly, as Kelsch and Kiéner[1] suggest, some relation to the intense renal congestion. The fever is often high, the temperature touching, in some instances, 41° C. (106° F.) or even higher.

The *urine* at the height of the process is of a deep brownish black color, and deposits on standing an abundance of reddish brown sediment. The amount varies considerably in different instances, in some being extremely scanty, in others amounting to as much as 1000 or 1500 c.c. The specific gravity varies inversely to the amount of urine passed. As the amount is generally somewhat reduced, the specific gravity averages above normal. The reaction varies; it is generally feebly acid. There is usually an abundance of albumin. In some instances a test for the biliary coloring matters may be obtained. Kelsch and Kiéner assert that this is the rule at the height of the process, while Plehn[2] in eight instances was unable to obtain this test. The sediment consists of mucus, bladder epithelium, numerous granules and masses of pigment, renal epithelial cells, and, almost invariably, hyaline and granular casts with epithelial cells adherent. In many instances blood-corpuscles may also be found, actual hemorrhages taking place into the kidney. Often, however, besides the profuse sediment of a brownish granular material, occasional epithelial cells, and casts, not a sign of a red corpuscle may be found, the condition being a true hæmoglobinuria.

In the simplest and mildest attacks the temperature remains elevated nine or ten hours, and then falls quite suddenly to normal, the urine at the same time clearing up, excepting for a slight trace of albumin with occasional casts. In some instances a paroxysm of this nature is the last manifestation of the process, complete recovery following. In other instances there may be repeated intermittent hæmoglobinuric paroxysms, ending perhaps in recovery. Very frequently, however, the condition is more severe. The fever lasts much longer; the vomiting and diarrhœa continue; the jaundice becomes more intense; there are perhaps occasional slight intermissions, but in the main the attack is continuous. The urine, as well as the fever, may show occasional temporary changes for the better, but these are of short duration, fresh exacerbations rapidly following. The urine becomes often scanty and more albuminous; the patient becomes emaciated and pale; the eyes are sunken, the tongue is dry, the pulse rapid and feeble, and eventually a fatal result follows. In some instances, however, recovery may occur when the patient is apparently almost beyond hope.

Certain cases pursue an extremely rapid fatal course. The initial chill, fever, vomiting, and diarrhœa are associated with almost complete suppression of urine; that which is passed, often but a few drops, is intensely bloody. There is great agitation, intense prostration, the patient falling into a condition of profound collapse and dying within several days. Nephritis almost invariably follows the hæmoglobinuric attack. In the milder cases it is transient and slight. In many more severe cases, however, the end of the paroxysm is followed by the symptoms of a well marked nephritis, lasting sometimes for weeks and possibly even for months. In a certain number of instances this condition pursues a rapidly fatal course. The albuminuria and casts persist; the quantity of urine remains steadily below normal; the patient becomes uræmic; and delirium, coma, and convulsions ensue with a fatal result.

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[1] *Maladies des Pays chauds.*

[2] *Deutsch. med. Woch.*, 1895, Nos. 25, 26, 27.

Malarial hæmoglobinuria does not occur in all malarious districts. In some regions where pernicious fevers are relatively common hæmoglobinuria is rarely seen. The cause for this is not apparent. In Rome, for instance, the disease is uncommon. It is not very frequent in most of the malarious districts of the United States. In Greece it seems to be unusually common, while in certain parts of Africa it is seen in its most fatal forms.

The *blood* generally shows the æstivo-autumnal parasite.[1] Predisposing causes appear to be any over-exertion or exposure, indeed anything which reduces the vitality of the individual. Extremely interesting is the widespread idea in certain regions that quinine, which has so specific an action upon the parasites, may yet have an unfavorable influence, indeed be the determining cause of the hæmoglobinuric paroxysm. In Joseph Jones' interesting memoirs[2] a number of assertions of this nature appear. More recently Plehn[3] in a valuable article upon the black water fever of Cameroon records his belief that in that climate, at least, the development of hæmoglobinuria is often brought about by the administration of quinine, while the records of his cases of hæmoglobinuric fever treated with and without the specific malarial remedy show that the more favorable course was pursued by those cases which were treated expectantly. This view, however, is not held by the majority of observers. The tendency toward spontaneous recovery in many of these cases suggests, certainly, that the presence of the hæmoglobinuria, dependent on whatever it may be, may have an injurious effect upon the life of the parasite.

THE BLOOD IN THE ÆSTIVO-AUTUMNAL FEVERS.—The blood in the æstivo-autumnal fevers shows the presence of the small form of the parasite described first by Marchiafava and Celli ("Hæmatozoön falciparum," Welch). As already noted in the description of the parasite, only the earlier forms in its cycle of existence are generally found in the peripheral circulation. These are the ring-like or amœboid hyaline bodies, which are often quite free from pigment. As the later stages in the development of the organism are rarely found in the peripheral circulation, it is natural that the period shortly before and during the early part of the paroxysm should be that in which the smallest number of parasites is to be found on clinical examination of the blood; and this is the case. There are cases of æstivo-autumnal fever where, at this period, a prolonged search must be made before parasites are to be found. Always, however, in the experience of the writer, parasites are present after a few hours have passed by. And I believe that it may be emphatically stated that there are no dangerous forms of malaria in which the parasite is not to be found after reasonably careful search.

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[1] This has been the case in those instances observed by the Roman authors, and the descriptions of Plehn and others seem to point in the same direction. Owing, however, to the remarkable distribution of these fevers, to which reference has been made above, we should perhaps bear in mind the possibility that there may be certain fine differences between the parasites of the ordinary irregular fevers and those of the hæmoglobinuric variety, which may be brought to light by further study.

[2] *Medical and Surgical Memoirs*, vol. ii., New Orleans, 1887.

[3] *Loc. cit.*

After the infection has existed for a week or two the crescentic and ovoid pigmented forms of the organism are usually observable. Phagocytosis is very commonly to be noted, and pigment-bearing leucocytes are to be found throughout almost all periods of the fever. The periodicity in the phagocytic action is much less marked than in the ordinary intermittent fevers. This is due in part to the presence at all times of parasites in different stages of development, and in part to the early necrosis of the red blood-corpuscles which is so common in these fevers the dead fragments are speedily engulfed and carried away by the colorless elements. Occasionally, true macrophages, such as are seen in the spleen, may be found in the peripheral circulation; these may be enormous, ten times the size of an ordinary leucocyte. They sometimes contain coarse granules, much larger than any ordinarily seen in the blood, having somewhat the appearance of eosinophilic granules. These cells may contain not only parasites, but red corpuscles, usually shrunken and brassy colored, including a parasite, and also entire smaller phagocytes with their included pigment or parasites or corpuscles.

FEVERS WITH LONG INTERVALS.—From the earliest times there have been described, besides the ordinary quotidian, tertian, and quartan intermittent fevers, other fevers with intermissions considerably longer; thus fevers with intervals of five, six, seven, eight, nine, ten, eleven, and twelve days, or even longer, have been believed to exist. Celsus, who distinguished quotidian, tertian, and quartan fevers, referred to the occasional occurrence of fevers with longer intervals, but noted their rarity.[1]

After Golgi's first researches concerning the life history of the quartan and tertian parasites, and after the fact became settled that a third variety of parasite existed, whose cycle, under some circumstances, lasted but twenty-four hours, the fever in every instance being definitely connected with the segmentation of a group of parasites, it is but natural that many observers should have suspected the existence of other varieties of parasites which in turn might be related to these rare fevers with longer intervals. And Golgi in 1889[2] advanced the hypothesis that the crescentic bodies which we know to be connected with the æstivo-autumnal parasite might bear a definite relation to these forms of fever. He believed that they represented a form of parasite which underwent a long, slow development, lasting from seven to twelve days—that, finally, segmentation of the crescentic forms occurred and paroxysms followed, just as in the case of the regularly intermittent fevers. This variety of parasite, however, differed in the greater length and the irregularity of the cycle of development, while the paroxysms, in like manner, recurred at irregular intervals, from seven to twelve days apart or even more. Canalis[1] believed that the æstivo-autumnal parasite possessed two separate cycles—a shorter, lasting from one to two days, and a longer, associated with the crescentic and ovoid bodies, lasting an indefinite length of time, three or four days at least. Antolisei and Angelini[2] also believed that this variety of parasite was associated with fevers with longer intervals.

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[1] "Interdum etiam longiore circuitû quaedam redeunt, sed id raro evenit."

[2] *Ziegler's Beiträge*, 1890, vii. 647.

Clinically, however, one very rarely observes cases showing a *regular* recurrence of paroxysms at intervals longer than every fourth day. On the other hand, it is not so very unusual to meet with cases where a number of paroxysms have recurred at intervals of, *approximately*, six to fourteen days. In all these instances one is generally compelled to depend largely upon the statements of the patient. An analysis of those cases which have been observed since the recognition of the parasite and its different varieties shows that these fevers with long intervals may be associated with any of the varieties of parasite which we now know. Golgi noted the existence of such paroxysms in patients whose blood showed the æstivo-autumnal parasite. Bignami[3] and Pes[4] described cases occurring in connection with the tertian parasite, while Vincenzi[5] has shown that they may be associated with the presence of any of the varieties of parasites which we now know, alone or in combination.

The manner in which these fevers arise was described first by Bignami. As stated in the description of the parasite, the mere presence of the organism in the circulating blood is not sufficient to produce subjective symptoms. These appear first only when, from steady multiplication, the number of parasites contained in the circulation has reached a certain necessary quantity. With every period of segmentation their number appreciably increases. Not every fresh segment, however, continues to develop. Were this the case, every infection would become pernicious within a short period. With each paroxysm a very considerable number of young parasites is destroyed—so great a number, in fact, that many, indeed the majority, of cases of tertian and quartan fever tend toward spontaneous recovery, though, to be sure, relapses often occur. To what this destruction is due is as yet a matter of doubt. In how far it may depend upon the protective power of the blood serum or upon an active defensive phagocytosis on the part of the leucocytes, or, possibly, upon the deleterious effects of some toxic substance produced, perhaps, by the parasite itself at the time of segmentation, is as yet wholly a matter of speculation. It is, however, not an infrequent occurrence to see, more particularly in tertian or quartan infections, a severe paroxysm followed by a complete disappearance of the symptoms, while the blood shows a disappearance of the group of parasites. The author has previously published charts of this nature.[6] In such instances, through some means or other, the greater part or an entire group of parasites is destroyed at the time of segmentation. In these cases the result is usually complete apyrexia for a certain length of time, from several days to two weeks or even more, and then, after, perhaps, a little warning, a repetition of the paroxysms.

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[1] *Fortschritte d. Med.*, 1890, Nos. 8 and 9.

[2] *Riforma Medica*, 1890, 320, 326, 332.

[3] *Ibid.*, 1891, No. 165, p. 169.

[4] *Ibid.*, 1893, vol. ii. p. 759.

[5] *Bull. R. Acc. Med. di Roma*, 1891-92, p. 631; *Arch. per le Sc. Med.*, vol. xix. f. 3, p. 263.

[6] *The Malarial Fevers of Baltimore, loc. cit.*

In some instances the first paroxysm may be followed by a period of apyrexia, lasting, as in one of the author's cases, eight days before the development of a second febrile attack, and that, in turn, by another intermission of approximately the same length of time, and so on, the chart thus showing an intermittent fever with intervals of, perhaps, eight or ten or twelve days. And yet the examination of the blood shows the characteristic parasites of tertian or of quartan fever.

The explanation, then, of these fevers with long intervals is not to be found in a parasite whose cycle of development lasts an unusually great length of time, but in the fact that the first sharp paroxysm is followed by the destruction of so great a number of the parasites that a long period—sometimes practically that of the period of incubation of the disease—must be passed through before the group again reaches a size sufficient to produce symptoms. The recurrent attacks represent, as Bignami pointed out, recrudescences from attacks from which complete recovery has not taken place. Single paroxysms with long intervals, or, more commonly, one or two paroxysms occurring together with long intervals between them, may exist for a very considerable length of time in tertian or quartan infections. Thus, the author has had occasion to observe an individual who for over two years had had occasional chills at irregular intervals of two or three weeks, more or less, due to an untreated tertian infection. One or two paroxysms were almost invariably followed by an apparent complete spontaneous recovery, only to be succeeded in the course of from two to four weeks by another relapse.

In another class of cases the paroxysms with long intervals are due to imperfectly treated malarial fever. Many patients living in malarious districts are in the habit of taking large single doses of quinine immediately following any outbreak of fever. Thus in an instance observed by the author a lady asserted that she had had paroxysms at intervals of ten days. The third or fourth paroxysm occurred under his observation, the blood showing the characteristic tertian parasites. In this instance the patient, by taking a single dose of quinine after each paroxysm, had accomplished the same end which nature accomplishes in the other class of cases—viz. the destruction of the greater part of the group of parasites; and in each instance a relapse occurred about ten days after the previous attack. The same explanation is probably true in the cases occurring in æstivo-autumnal infections. There is no evidence to show that there is any such thing as a regular type of fever occurring at intervals longer than every fourth day. The paroxysms in these instances differ in no way from those in tertian, quartan, or æstivo-autumnal fevers according to the variety of infection.

COMBINED INFECTIONS WITH DIFFERENT VARIETIES OF PARASITES.

Combined infections with two or more varieties of the malarial parasites may occur, though they are rather uncommon. In 542 cases of malarial fever classified by Hewetson and the author there were only 11 such instances. Clinically, these cases present usually the features of an ordinary tertian, quartan, or æstivo-autumnal infection, and without examination of the blood the presence of two varieties of parasites would often remain unsuspected. This is due to the fact that the two different varieties of the organism are rarely present each in sufficient number to produce symptoms at the same time. One type of the parasite almost always predominates, and is responsible for the clinical symptoms. Certain cases have been noted where a distinct alternation of symptoms has occurred; a period of quartan fever, for instance, being followed by spontaneous recovery, and succeeded by a period of tertian fever, which, if untreated, pursues the same course, and gives way finally to a relapse of the quartan infection; the parasites of both varieties are present at the same time. In rare instances complicated fever curves may arise from a combined infection. This is, however, very unusual. The commonest combination in this climate is æstivo-autumnal and tertian fever.

THE URINE.—The urine in the malarial fevers has no special diagnostic features. There are no constant changes in the *amount* or in the *specific gravity* of the twenty-four hours' urine. The *color* of the urine is somewhat increased, due probably to the increased quantity of urobilin which is derived from the hæmoglobin of the red blood-corpuscles destroyed by the parasites. The amount of *urea* excreted during the paroxysms is increased, just as it is during any other acute febrile condition. *Albumin* is usually present in serious cases. Thus, out of 284 cases examined by Hewetson and the author, albumin was present in 133 instances, nearly one-half. In many of these instances casts of the renal tubules may be found. Actual *acute nephritis* may occur. Thus in 4 instances out of 335 of our cases evidences of a severe acute nephritis were present—a nephritis which, apparently, owed its origin directly to the malarial infection. In 3 of these instances the nephritis was hemorrhagic in nature; in the other case, which resulted fatally, there was an extensive acute diffuse nephritis. Ehrlich's diazo reaction may be present; it was found in 5.5 per cent. of our cases.

The Toxicity of Malarial Urine.—Extremely interesting researches have lately been made concerning the increased toxicity of the urine during malarial fever. Brousse,[1] studying the effects following the injection of the urine of cases of malarial fever into animals, arrived at the following conclusions: "(1) The urotoxic coefficient calculated by Bouchard's formula, the mean coefficient being 0.464, rises during the paroxysm, and the physiological effects observed are those which usually follow the injection of urine—dyspnœa, myosis, falling of temperature, exophthalmos, and furthermore convulsions; (2) this toxicity is diminished during the period of convalescence in intermittent fever, very much below that of the urine during the paroxysm, and moreover below that of the normal urine."[2]

Roque and Lemoine[3] studied the urine in 3 cases of malarial fever—one a case of tertian fever and two cases of pernicious comatose malaria. Their conclusions were as follows: "(1) The pathogenic agents of paludism form, in the blood, a large quantity of toxic products, a great part of which is eliminated by the urine. This elimination is at its maximum immediately after the paroxysm, and lasts, generally, twenty-four hours, at least in the paroxysms of tertian fever. (2) Sulphate of quinine acts by favoring the increase of this elimination. (3) Certain pernicious fevers, showing a complete absence of toxicity in the urine, depend probably upon alterations in the kidneys and liver, and the return of the urinary toxicity should be considered a good prognostic sign. (4) Finally, it may be noted that in two cases recovery has followed a more increased elimination of toxines than that observed after the preceding paroxysms." In discussing this paper Lépine justly remarked that injections should be made not only with the pure urine, but also with a solution of the salts of the urine made after calcination. This alone can give a reliable idea of the toxicity of the urine dependent upon organic compounds.

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[1] Quoted from Laveran, *Du Paludisme, etc.*, Paris, 1891.

[2] *Société de Méd. et de Chir. pratiques de Montpellier*, 14 Mai, 1890.

[3] *Revue de Méd.*, 1890, p. 926.

More recently Botazzi and Pensuti[1] have made an elaborate control research, and, while finding the same general results as Roque and Lemoine, dispute their conclusions. Their studies were carried out in ten cases. They collected urine during and after the febrile periods. They found that during the paroxysm the urine showed a less intense color than afterward. During the febrile periods examination of the urine with the ordinary reagents which are used in qualitative analysis showed always a diminished amount of alkaline and earthy phosphates, while that voided after the paroxysm showed sometimes a considerable quantity. The specific gravity of the urine passed after the paroxysm was higher than that during the paroxysm. They state that under other conditions the urotoxic coefficient has been shown to run parallel to the elimination of the potassium salts, while the presence of peptones in the urine increases appreciably its toxicity. Both these substances they found present in increased quantities in the urine passed after the paroxysm. The urobilin, as already stated, is present in increased quantities in the urine of malarial fever, and especially so in that following the paroxysm. The toxicity of this substance has been demonstrated by these authors, who found that the urine passed after the paroxysm, when decolorized, lost half its toxicity. They assert, in opposition to Roque and Lemoine, that "there is no need to suppose the presence of special toxic substances of the nature of leucomaïnes to account for the toxicity of malarial urine" [after the paroxysm]; "the potassium, the phosphoric acid, the peptones, the urinary pigments, and especially urobilin, which are found in this urine in markedly increased quantities relatively to the normal urine and to that of the febrile period, are of themselves a sufficient explanation." The cause of the increased presence of these substances is not difficult to appreciate. The potassium salts and the pigments which they believe to be the chief cause of the hypertoxicity result from the destruction of the red blood-corpuscles, and the phosphoric acid and peptones are doubtless due to the disintegration and combustion of the albumins and nucleins of the cellular elements of the tissues. They have not found evidence of a marked retention of toxic substances owing to disease of the kidneys, as asserted by Roque and Lemoine.

In conclusion, they state: "We think that we have demonstrated (1) that in the malarial fevers the febrile urine is less toxic than that emitted during the apyretic stage; (2) that the urine emitted during the period of apyrexia is more toxic than normal urine; (3) that the toxicity of the urine of malarial patients augments constantly with the succession of febrile attacks, though in some cases this augmentation appears in the form of unexpected and irregular exacerbations; (4) that, as there is nothing specific in the course of the intoxications produced in rabbits with malarial urine, there is no need to suppose the presence of specific toxins or substances of the nature of leucomaïnes, for the salts of potassium, phosphoric acid, the urinary pigments, the peptones, all of which substances are eliminated in increased quantities, are a sufficient explanation; (5) that the injection of febrile urine is followed by a slower intoxication, characterized by sopor, by increased diuresis, by diarrhœa, and mydriasis, while the apyretic urine produces a more acute effect, sometimes fulminating, characterized by clonic and tonic spasms and myosis, '*exhorbitisme*,' spastic expiration; (6) that to explain this different picture one may suppose that with febrile urine the polyuria and diarrhœa are due chiefly to the increased richness in the urea, while the peptones may contribute to the production of sopor. In the afebrile urines the salts of potassium, the phosphoric acid, the urinary pigments, and especially the urobilin, manifesting themselves as substances essentially convulsive, determine hypertoxicity. (7) Finally, besides the hæmocytolysis and the destruction of the cellular elements of the tissues, and the formation and elimination of toxic substances, there must exist intermediate factors which account for the absence of increased toxicity after the first febrile paroxysms and the irregular elevation and diminution in the urotoxic coefficient in some other cases." Laveran speaks also conservatively concerning these experiments as a proof of the existence of a specific toxin.

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[1] *Lo Sperimentale*, Firenze, 1894, xlviii. 232, 254.

In conclusion, then, one may say that while a distinct increase in the toxicity of the urine has been shown to be present after malarial paroxysms, there is as yet no proof that this is dependent upon specific products of the action of the malarial parasite.

THE BLOOD.—Besides the presence of the parasites, the examination of the blood in malarial fever reveals certain other changes which are at times valuable from a diagnostic point of view.

(A) *The Regularly Intermittent Fevers.*—An actual *anæmia* always occurs in malarial fever. Kelsch,[1] Kalindero,[2] Dionisi,[3] all noted that a considerable fall in the number of *red blood-corpuscles* to the cubic millimetre occurred after each paroxysm, while similar results were obtained by Dr. Kirkebride in some counts made under the author's observation in 1893. The fall in the number of red corpuscles may be quite considerable, though in tertian and quartan fever the restitution to normal is very rapid. Always, however, after several paroxysms have occurred there is a certain degree of anæmia, which, if the disease be allowed to continue, may become quite marked.

The percentage of *hæmoglobin* falls with the number of corpuscles, but usually to a somewhat greater extent, while the return to the normal point, as noted by Rossoni,[4] takes place more slowly than that of the red corpuscles.

[1] *Arch. de Phys.*, 1876, ii. s., t. iii. 490.

[2] *Jour. de Méd. et de Pharm. d'Algérie*, 1889, xiv. 123.

[3] *Lo Sperimentale*, 1891, t. iii. and iv. 284.

[4] *Lav. d. Cong. d. Soc. Ital. d. med. Int., II° Congresso*, Roma, Oct., 1889, 121.

The behavior of the *colorless corpuscles* in malarial fever has been noted especially by Kelsch,[1] Kalindero,[2] Bastianelli,[3] and Billings.[4] It has been shown that the number of leucocytes in malarial fever is almost invariably subnormal. The smallest number of leucocytes is seen just after the paroxysm when the temperature is subnormal. From this time there is a gradual, slight increase, which becomes accentuated just before the paroxysm. A rapid diminution in number occurs again during the paroxysm. At no time is there leucocytosis.

(*B*) *The Æstivo-autumnal Fevers.*—The changes in the blood in the æstivo-autumnal fevers are very similar to those in the regularly intermittent forms, differing only in their intensity. The red corpuscles show a marked diminution with each paroxysm. When the parasites are numerous this reduction amounts, sometimes, to as much as a million corpuscles during a single paroxysm. Between the attacks the corpuscles do not show the same tendency to return to the normal number which is observed in the regularly intermittent fevers. The restitution is imperfect and incomplete. The number, however, rarely falls below one million to the cubic millimetre, although Kelsch has seen as small a number as five hundred thousand. The *colorless corpuscles* are almost invariably reduced in number. The changes in number follow the same course here as in the regularly intermittent fevers. There is a diminution after the paroxysm, a slight rise just before the beginning of the succeeding attack, with a fall again later on. The *hæmoglobin* follows the same curve as do the red corpuscles, falling, however, generally to a slightly greater extent.

In certain instances a well marked leucocytosis has been noted in pernicious paroxysms. Bignami has noted the unfavorable inferences that one may draw from this symptom. In some instances this, very possibly, depends upon a secondary mixed infection. In other instances, however, it may occur where cultures from the organs are quite negative. Thus, in one of the author's cases of the pernicious algid type the blood contained, one hour before death, sixty thousand leucocytes to the cubic millimetre. The leucocytes in malarial fever show certain other changes which are quite characteristic and interesting. Just as in the case of typhoid fever, where the number of leucocytes is ordinarily subnormal, so in malarial fever, one finds upon a differential count a well marked reduction in the percentage of the polymorphonuclear neutrophiles, with a corresponding relative increase in the percentage of the large mononuclear forms. Thus the average numerical proportions of the various forms of leucocytes in sixteen cases analyzed in this clinic by Billings were as follows:—

Small mononuclear	16.9
Large mononuclear	16.9
Polymorphonuclear	65.04
Eosinophilic	0.96

In the pernicious case above referred to, observed by the author, the relative proportions of the different varieties of leucocytes, notwithstanding the leucocytosis, were as follows:

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[1] *Arch. de Phys.*, 1876, ii. s., t. iii. 490.

[2] *Loc. cit.*

[3] *Bull. d. R. Acc. Med. d. Roma*, 1890, Anno xviii., f. v. 297.

[4] *Johns Hopkins Hospital Bulletin*, 1894, No. 43, 105.

Small mononuclear	23	per cent.
Large mononuclear and transitional forms	18.4	"
Polymorphonuclear	58.6	"

The changes in the blood in malarial hæmoglobinuria have been already referred to.

The grave anæmiæ which may follow malarial fever will be considered later among the sequelæ.

SEQUELÆ AND COMPLICATIONS.

There is no one point in the history of the development of our knowledge concerning the malarial fevers where so much confusion and misapprehension has existed as in the appreciation of the nature of the sequelæ and complications. The relation of chronic cachexia and grave anæmia to malaria has long been recognized, as well as the existence of an acute post-malarial nephritis. The grave cerebral, nervous, gastro-intestinal symptoms which may occur with acute malaria have been already referred to. Many observers, however, do, even today, ascribe to the malarial poison the capacity of producing of itself a considerable number of other complicating processes ordinarily dependent on other specific causes. These observers have in particular described a characteristic "malarial pneumonia," "malarial dysentery," etc. That such misapprehension should have arisen is not remarkable when we consider the many ways in which the simple malarial process may be masked or complicated.

Ascoli[1] states clearly the main possibilities in this direction as follows: "Finally, in conclusion, we may distinguish the following clinical forms: (1) Malaria which simulates another pathological process. (2) A disease, the [ordinary] course of which is known, which, in an individual suffering with chronic malaria, progresses and develops anomalies in its course according to the stage of the cachexia.[2] (3) A fresh malaria develops in a subject who is at that time in an apyretic stage of the disease or suffering from the remains of a former infection (*combinata*). (4) Different varieties of the hæmatozoa exist in the blood of a patient suffering from malaria alone (*mista*). (5) Two febrile diseases exist together and contemporaneously (*concomitanti*): (*a*) exerting a reciprocal influence detrimental to the organism (*proporzionate*); in certain of these cases the reciprocal influence is not manifest throughout the entire course; (*b*) each preserving its more constant and common symptomatology (*associata*). (6) The malaria may prepare the ground for the development of another acute infection, or it may follow after another infection has run itself out (*consecutiva*)."

The sequelæ and complications of malarial fever may be divided into—(1) Those sequelæ or complications due directly to changes produced by the malarial parasites or their toxic products; (2) true complications, mixed infections.

1. **Sequelæ and Complications due directly to Changes produced by the Malarial Parasites or their Toxic Products.**—In the section upon the pernicious fevers the acute symptoms produced by the special

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[1] *Bull. della Soc. Lanc. d. Osp. di Roma*, An. xii., 1891–92, 103.

[2] "Una malattia di processo morboso noto che, attacando un malarico chronico, assume andamento e parvenze variabili secondo lo stadio della cachessia."

localization of the parasites in the brain, lungs, or gastro-intestinal tract have already been discussed. It is therefore unnecessary to refer again to the acute choleriform and comatose cases which might so readily suggest a mixed infection.

RELAPSES.—The extreme frequency with which relapses are met in malarial fever has been referred to in the section on fevers with long intervals. Most cases, unless treatment be thoroughly carried out, show recrudescences in the course of one or two or three weeks. These are clearly proven to be due to the fact that all the parasites have not been destroyed by the treatment. The few which escape form a nucleus for the development of new groups, which in the course of a week or two arrive at a degree of development sufficient to result in a fresh outbreak of the symptoms. The recrudescences are, ordinarily, in every way similar to the original attacks. There is, however, another variety of relapse which has been recognized for many years—viz. the reappearance of an infection many weeks or months after all symptoms have disappeared. Undoubtedly, many such cases are fresh infections. There are, however, cases where a fresh infection can be definitely ruled out, while the malarial nature of the process is undoubted. An interesting example of the reappearance of fever after a long period of perfect health is the case of a friend of the author, a physician himself, wholly familiar with malarial fever, clinically and pathologically. During the fall of 1880 Dr. —— suffered from a prolonged attack of tertian fever which reduced him to rather a cachectic condition. Recovery followed full doses of quinine. For twenty-one months after this the health was perfectly good, the patient living in non-malarious districts. On a hot afternoon of August, 1882, while making a pedestrian tour in the Tyrol, after a prolonged walk, during which the patient was subjected to great changes of temperature, there was a well defined characteristic malarial paroxysm. The true nature of the attack was not suspected, but on the third day, at the same hour, while travelling in a railway-carriage, there was a second paroxysm. On the fifth day, again, at the same hour, a third characteristic paroxysm occurred. Convinced then of the malarial nature of the attacks, treatment with quinine was begun, which resulted in the immediate and permanent disappearance of the paroxysms. In the words of Dr. ——, "In this case there can be no question of a second infection. I had not been in a country where there was any malaria for two years, and for three weeks before the appearance of the first chill I had been in the mountains of the Tyrol."

The absolute proof—the discovery of the parasite—is here wanting; there can be little doubt, however, as to the nature of the case. The explanation of these cases is difficult. It is highly improbable that the parasite has remained present in the blood, passing through its ordinary cycle of development, and yet some form of the parasite must exist throughout this time. Bignami, as was noted in the description of the parasite, suggests that some form of the organism—which perhaps we have not yet been able to discover, possibly a non-staining spore—may persist in some of the internal organs, possibly within the protoplasm of some of the cellular elements.

CHRONIC MALARIAL CACHEXIA.—The commonest sequel to malarial fever is that which is generally known as chronic malarial cachexia.

may be rapid and fatal; in the majority, however, the prognosis is favorable and complete recovery occurs. It is not impossible that, in some instances, a fatal chronic diffuse nephritis may owe its origin to the malarial poison; however, definite proof of this is as yet wanting. There is nothing absolutely characteristic, clinically or pathologically, in these instances of malarial nephritis.

AMYLOID DEGENERATION.—Amyloid degeneration is an occasional sequel to malarial fever. Two cases were reported by Frerichs,[1] and several others have recently been studied by Marchiafava and Bignami.[2] These cases have followed after a long series of febrile attacks, those which have been carefully studied having been æstivo-autumnal or obstinate quartan fever. The clinical symptoms are those of nephritis accompanied by an extremely rapid cachexia, ending fatally, as a rule, within several months. The blood in these cases may show the condition first noted by Ehrlich as of grave portent—viz. complete absence of nucleated red corpuscles and eosinophilic cells, and reduction in the number of the leucocytes, with an excess of lymphocytes, while at autopsy the marrow of the long bones is found to be entirely fatty, showing no evidence of an attempt at proper regeneration.

ATROPHY OF THE GASTRO-INTESTINAL MUCOSA.—Pensuti[3] has reported a case of extensive atrophy of the gastro-intestinal mucosa following, apparently, an acute malaria. Constant diarrhœa followed the attack, resulting in great exhaustion and death from broncho-pneumonia in three months. Though Baccelli was inclined to believe that the change was directly due to the action of some toxic substance connected with the malarial infection, the case cannot be said to be wholly convincing.

MALARIAL HEPATITIS; MALARIA AND CIRRHOTIC PROCESSES.—As has been stated in the section on *Pathological Anatomy*, many observers insist upon the occurrence of a true atrophic cirrhosis of the liver as a sequel to malarial fever. There are many reasons which would lead us to believe that this may, in some instances, occur, but clinically, in this climate at least, such cases are rarely met with. In few instances does one meet with a true atrophic cirrhosis of the liver in which other important etiological factors have not also been present. No such case has come under observation in the Johns Hopkins Hospital in the seven years since its opening. On the other hand, chronic hepatitis, resulting usually in an increase in the size of the liver, is commonly observed in malarial cachexia and following repeated malarial infections. Distinct clinical symptoms due to the hepatic changes do not apparently exist.

MALARIAL PARALYSES.—*Cerebral Paralyses.*—Various paralyses have been described in association with malaria. The different forms which may occur in acute pernicious malaria have already been referred to. They are usually transitory, disappearing under treatment, and are due probably to circulatory disturbances induced mechanically by the parasites: they are almost always cortical in nature. The nervous symptoms in acute malaria are more commonly irritative than paralytic.

Occasionally symptoms suggesting involvement of the *spinal cord* grayish yellow, parchment-like skin hangs in folds; the mucous membranes are blanched. There are occasionally slight febrile attacks, the child becoming cold and blue, or, perhaps, showing now and then a slight eclamptic attack. There are persistent gastro-intestinal disturbances, vomiting, diarrhœa, as well as, perhaps, diffuse bronchitis. The spleen is always enormously enlarged.

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[1] *Loc. cit.*

[2] *Loc. cit.*

[3] *Gaz. Med. di Roma*, 1893, xix. 121.

POST-MALARIAL ANÆMIA.—The anæmia associated with malarial fever may assume various forms. Thus, Bignami and Dionisi[1] have distinguished four types of post-malarial anæmia.

(1) Anæmia, in which the examination of the blood shows alterations similar to those observed in ordinary secondary anæmia, differing from these cases only in that the leucocytes are diminished in number. These cases often show well marked oligocythæmia; oligochromæmia relatively greater; more or less poikilocytosis; nucleated red corpuscles (normoblasts). The leucocytes, as already stated, are diminished in number, while the relative proportion of the large mononuclear forms is increased at the expense of the polymorphonuclear cells. The greater number of these cases go on to recovery; a few, however without any change in the hæmatological condition, pursue a fatal course.

(2) Anæmia in which the blood shows changes or alterations similar to those common in pernicious anæmia—*i. e.* marked oligocythæmia; oligochromæmia relatively less; marked poikilocytosis; nucleated red corpuscles, for the most part gigantoblasts; leucocytes, diminished in number with an increase often in the small mononuclear forms, and a diminution in the polymorphonuclear varieties. These cases end fatally.

(3) Anæmia showing the ordinary characteristics of secondary anæmia, excepting for the complete absence of regenerative forms (nucleated red corpuscles). These cases are progressive and fatal, the marrow, at autopsy, showing, as has already been stated, no evidence of regenerative activity.

(4) Chronic secondary anæmiæ occur in prolonged cases of malarial cachexia, and are remarkable for the small number of nucleated red corpuscles present and the marked reduction in the number of the leucocytes, particularly of the polymorphonuclear variety. There are, however, post-malarial anæmias which do show after the clearing up of the infection a leucocytosis similar to that in ordinary secondary anæmia. This is probably a favorable sign, pointing to a rapid regeneration.

MALARIAL NEPHRITIS.—The grave damage which the kidneys may suffer in certain acute malarial infections, either from the direct action of some toxin produced by the hæmatazoa or from the presence in the circulation of injurious substances, due indirectly to the action of the parasite, is most strikingly brought to one's notice in the intense acute nephritis which, as described in a previous section, may follow malarial hæmoglobinuria. The kidney, however, rarely escapes a certain amount of damage in any severe malarial infection. Thus, out of 284 cases analyzed by Hewetson and the author, albumin was found in nearly one-half, while severe acute nephritis was present in 4 instances. The nephritis following malarial fever is usually a mild acute, diffuse process similar to that observed in any infectious disease. In some instances, as stated in the section on malarial hæmaturia, the course may be rapid and fatal; in the majority, however, the prognosis is favorable and complete recovery occurs. It is not impossible that, in some instances, a fatal chronic diffuse nephritis may owe its origin to the malarial poison; however, definite proof of this is as yet wanting. There is nothing absolutely characteristic, clinically or pathologically, in these instances of malarial nephritis.

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[1] *Loc. cit.* [2] *Loc. cit.*

[3] *Gaz. Med. di Roma*, 1893, xix. 121.

All of these processes coming on with acute malarial fever are essentially favorable in their course if treatment be begun in time. According to Boinet and Salibert, however, permanent paralyses, both cerebral and spinal in nature, may follow malarial fever.

Cases of *peripheral neuritis* following malarial fever have been reported, though definite proof that they were malarial in origin has not been obtained. From what we know, however, of the pathogenesis of the disease, we may readily believe that malarial fever as well as other acute infectious diseases, may be followed by acute degenerative lesions in the peripheral nerves.

Some observers have believed that there was some predisposing relation between malarial fever and *Raynaud's disease* (symmetrical gangrene), though this is by no means proven. Poncet has described a retinitis and a *retino-choroiditis*, due to emboli of melaniferous leucocytes in the capillaries.

MENTAL DISEASES.—Various mental affections may follow malarial fever, just as may be the case with any acute infection. There is nothing especially characteristic in these cases. Thus, one of our instances of tertian malaria was followed by an attack of paranoia lasting for several months.

True Complications and Mixed Infections.—Malaria, like any other acute disease, is subject to various complications, many of which are a result of mixed infections with other pathogenic agents. As stated before, many of the symptoms caused by mixed infections were believed by the older observers to be due directly to the malarial poison. Of late, however, with our increased facilities for study and appreciation of these conditions, it has been recognized that in the majority of instances the complication is dependent upon a true mixed infection.

PULMONARY COMPLICATIONS.—PNEUMONIA.—As has been stated

[1] *Bull. d. Soc. Lanc. d. Osp. d. Roma*, 1891, xi. 217.
[2] *International Clinics*, Philada., 1891, iii. 246.
[3] *Beiträge z. Pathologie u. Pathologischen Anatomie des Centralnervensystem*, Leipzig, 1879.
[4] *Bull. d. R. Acc. Med. di Roma*, 1893-94, Anno xx. p. 221.

in an earlier section, many observers have described pernicious fevers which during the paroxysm showed well marked pulmonary symptoms, dyspnœa, pain, hæmoptysis. These symptoms, dependent probably upon the special localization of the parasites in the pulmonary capillaries, are to be sharply distinguished from true pneumonia, which may, and not unfrequently does, complicate a malarial attack. Again, in certain instances an ordinary acute pneumonia may present an intermittent fever which simulates quite closely the chart of intermittent malarial fever. These cases, however, may be readily recognized by the absence of the parasite from the circulating blood. Such cases have been described by Wunderlich, Jaccoud, Bertrand, and Andrew Clark, while Ascoli[1] gives an excellent chart. True acute pneumonia and malarial fever may, however, coexist. In these instances the course of the pneumonia may be but little influenced by the coexisting malarial fever, while in other instances the exacerbations and remissions of temperature may be quite marked. Here the pulmonary process is a genuine croupous pneumonia, due, as has been shown by Marchiafava and Guarnieri,[2] to infection with the diplococcus lanceolatus. Its course is quite uninfluenced by the administration of quinine, and its connection with malarial fever is purely accidental, unless, as it may be in some instances, a preceding malaria has prepared the ground for the pneumococcus infection by reducing the vital forces of the individual. Pneumonia occurring in individuals suffering with chronic malarial cachexia appears to pursue an unusually malignant course, owing, doubtless, to the reduced condition of the patient. Retarded resolution and "organization" of the exudate are not uncommon in these instances (Ascoli). *Broncho-pneumonia* is also occasionally observed in association with malaria. The infection, however, is purely secondary, in no way directly related to the malarial process.

PLEURISY.—Certain observers have described symptoms in acute pernicious malaria suggesting pleural involvement where, on autopsy, nothing was to be found. In other instances pleurisy and malarial fever may coexist, although there is nothing whatever to show that this pleurisy is not an entirely separate process from the malarial infection. There is nothing abnormal in the clinical or pathological course of such a pleurisy; it is uninfluenced by the administration of quinine. These cases are not to be confounded with the pleural transudations which may occur in cachectics. Quinine has no influence upon the process.

TYPHOID FEVER.—The relations between malarial fever and typhoid fever have been much discussed, and are today probably more generally misunderstood in this country than any one point in connection with the febrile diseases. Since the discovery of the malarial parasite, with our modern means of diagnosis, there is no reason for the existence of any such confusion at the present day. The great similarity between the symptoms in certain cases of æstivo-autumnal fever with typhoid fever has been pointed out in earlier sections. There is, however, no excuse whatever for the physician who today fails to recognize the malarial nature of such a fever after a few days' observation. The simple examination of the blood will invariably settle this question, the parasite being always present.

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[1] *Loc. cit.*

[2] *Bull. d. R. Acc. Med. di Roma*, xv. 1888-89, 355.

Few are unfamiliar with the term so commonly employed, "typho-malarial fever." It was supposed that in malarious districts there existed a continued fever which depended upon the combined action of two poisons, that of malaria and that of typhoid fever—true "*proportionata*," in the sense of the old Italian observers. This fever was supposed to be markedly resistant to quinine and to betray its malarial nature by the frequency with which rigors occurred. We know today that "typho-malarial fever" as a distinct entity does not exist. Rigors occurring in the course of typhoid fever are by no means uncommon, but are of themselves wholly insufficient evidence on which to base a diagnosis of malaria. We know, on the other hand, that there exist, in this country at least, no malarial fevers which resist for more than three or four days the action of quinine. True complications of typhoid fever and malaria may occur, but they are rare, only one doubtful instance having been observed in seven years in the Johns Hopkins Hospital, where both typhoid fever and malaria are, unfortunately, very common. Typhoid fever may be acquired by a patient suffering from acute or chronic malaria. A fresh malarial infection may break out or a slumbering infection may come to life again during the course of typhoid fever. But this condition is uncommon, and in no way justifies the term *typho-malarial fever*. There is little doubt that the enormous majority of cases referred to today as "typho-malarial" fever in this country and elsewhere are cases of typhoid fever, pure and simple. Too much stress cannot be laid upon this point, for the groundless assumption that there exists in this country a fever due to the combined action of typhoid and malarial poison, pursuing a fairly characteristic course and calling, from its malarial nature, for the continued use of quinine, has exercised in the past, and is exercising today, an extremely injurious influence upon the medical practice of this country. This influence cannot fail to be appreciated by the intelligent observer who has occasion to note the quantities of quinine which are systematically administered to many cases of uncomplicated typhoid fever in various districts of the United States.

In the instances of true mixed infection of typhoid and malarial fever the picture may be most varied. If a fresh malarial attack or a relapse break out during the course of typhoid fever, well marked indications of the paroxysms, varying according to the type of parasite present, may be observed, as shown admirably by the charts recently published by Gilman Thompson.[1] In these instances the blood shows the presence of the parasites; these, with the symptoms dependent upon them, disappear immediately after ordinary doses of quinine. If, on the other hand, the typhoid fever develop in the course of latent or chronic malarial infection, the symptoms on the part of the malarial parasite may be almost absent.

INTESTINAL COMPLICATIONS.—The occurrence of diarrhœa, particularly in children, during acute paroxysms is well known. The changes produced by the malarial parasite in the intestine in certain acute pernicious cases have already been considered; the acute choleriform pernicious paroxysm is truly malarial in nature. There is nothing, however, to show that the more chronic dysenteries and diarrhœas often associated with cachexia are in any way directly connected with the action of the malarial poison, excepting in so far as this may have prepared the ground. It is not impossible to conceive that severe infections might follow directly upon an acute choleriform attack. Particularly interesting are several cases noted in the medical clinic of the Johns Hopkins Hospital, where the *Amœba coli* has been found in the dejecta of patients suffering simultaneously with acute malaria and dysentery. In all of these instances the intestinal process might well have been directly ascribed to the malarial poison. The frequency with which the Amœba coli is associated with tropical dysenteries makes it exceedingly probable that many of these post-malarial intestinal affections in tropical climates may be in reality due to a mixed infection with the two protozoa, as in our instances.

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[1] *Trans. Ass. Am. Phys.*, 1894, 110.

Tuberculosis.—Numerous observers, and particularly Boudin,[1] have asserted that tuberculosis was directly antagonistic to malarial fever and the converse. Boudin pointed out that tuberculosis was rare in countries where malaria existed, and that where tuberculosis was common malaria was rare. This assumption has exerted a certain influence on the minds of many. Experience, however, has shown that it lacks foundation. In many of the districts where malaria is common it is true that tuberculosis is unusual, owing to certain climatic influences. In the northern regions, where tuberculosis is more common, malaria, as is well known, is relatively infrequent. In other regions we find malarial fever and tuberculosis side by side, intimately associated, occurring, by no means infrequently, in the same patient. Marchiafava,[2] indeed, is inclined to believe from his observations that chronic malaria is not an unimportant predisposing cause to pulmonary tuberculosis. It is, however, really interesting that among the 614 cases analyzed by Hewetson and the author in not a single instance was pulmonary tuberculosis present.

Other Infections.—Infection with the other pathogenic organisms is not so very rare; thus the author has observed *furunculosis*, *parotitis*, *tonsillitis*, and *acute rheumatism*, while in one fatal case, admirably studied by Barker, there was a general infection with the *Streptococcus pyogenes*. Antolisei and Laveran have observed cases of *variola* complicated during convalescence by characteristic malarial fever, while Baccelli has observed the same in cases of other *exanthemata*.

Post-partum and Post-operative Malaria.—One hears not infrequently of post-partum and post-operative malarial fever, and it is, alas! only too common today to ascribe elevations of temperature during the first few days after operation and during the puerperium to malarial fever. This condition is probably rare. There are few such instances in literature where the malarial nature of post-partum paroxysms was definitely proven. In the seven years since the opening of the Johns Hopkins Hospital not a single case of post-operative malaria has occurred. Undoubtedly, the reduced condition of the patient during these periods might, and probably does, favor a recrudescence of the latent malarial infection. It is, on the other hand, probable that the majority of instances of supposed post-partum and post-operative malaria have no connection whatever with true malarial fever, but represent simply a septic infection. This has been the case in every instance of suspected post-operative malaria which has come under the author's observation.

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[1] *Traité des Fièvres intermittentes*, Paris, 1842.

[2] *Bull. d. Soc. Lanc. d. Osp. d. Roma*, 1891, Anno xv. 186.

INSOLATION.—The complication of an active or chronic malarial fever with insolation is probably not very uncommon. Bastianelli and Bignami[1] have recently demonstrated in an interesting manner the frequency with which such cases have, in Italy, been considered as essentially malarial in nature. The pernicious malarial fevers are particularly common at the hottest season of the year, while the individuals most subjected to malarial infection are also often those who work bareheaded in the fields, exposed directly to the sun's rays. These observers called attention to the fact that a number of instances of what has been considered pernicious comatose malaria have been reported in which, at autopsy, only cerebral hyperæmia, pulmonary hypostasis, and slight degenerative changes in other organs were observed. In some of these cases no malarial parasites were to be found; in others, evidences of a recent infection; in others, perhaps the evidence of a recent infection with the presence of a small number of active parasites—far too few, however, to account under ordinary circumstances for such grave symptoms. Cases of this nature have led some observers to assume that a very small number of parasites might give rise to severe pernicious symptoms, owing to their excessive malignancy. It is much more probable, as Bastianelli and Bignami state, that the process represents a complication of malarial fever with insolation which might occur in an individual with active malarial fever or in one who has recently recovered from an attack. Indeed, it is not impossible that a preceding malarial infection, by reducing the strength of the individual, may render him more subject to such attacks.

DIAGNOSIS.

(1) THE REGULARLY INTERMITTENT FEVERS.—The diagnosis of the regularly intermittent, tertian, and quartan fevers is generally a relatively simple matter. The regular paroxysms with their three stages of chill, fever, and sweating are so characteristic as to leave little doubt in most instances concerning the nature of the process. The anæmia and the enlarged spleen which are present in the vast majority of instances are also important from the point of view of differential diagnosis. Occasionally paroxysms very closely similar to the malarial access may occur from other infectious causes, and sometimes the regularity with which the individual paroxysms may succeed one another may lead to errors in diagnosis. The paroxysms, however, in malaria differ in certain respects from those occurring in most other acute infections. Thus, the average duration of the malarial paroxysm, if we estimate the course from the time the temperature passes 99° until it again falls below this point, is from ten to twelve hours, while in other infections the course is often materially shorter. There may, of course, be mild malarial paroxysms which last but four or six hours, but in these the temperature is correspondingly moderate. One rarely observes in malarial fever temperatures of 104°, 105°, or 106° in a paroxysm lasting as short

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[1] *Bull. d. R. Acc. Med. d. Roma*, 1893–94, Anno xx. p. 151.

a time as six hours or even less. The writer has seen cases of septic infection in which, for a considerable length of time, chills closely simulating those of malarial fever occurred, while the anæmia and enlarged spleen were also present. The chief difference to be noted was the marked difference in the length of the paroxysms, which were sometimes as short as four or five hours, the temperature reaching, perhaps, within this time a point as high as 106°. The same may be true of the chills which are not so infrequently seen during the course of typhoid fever—chills caused, doubtless, by auto-intoxications as yet not understood. Whenever the temperature rises as high as 104° and the paroxysm lasts no longer than six hours, one is justified in the suspicion that the fever is not malarial in origin.

At times, however, other infections may give rise to paroxysms most closely simulating those of malarial fever. Thus, in two instances the writer has observed typical quotidian paroxysms lasting from ten to twelve hours, and beginning nearly at the same hour on two successive days, which were considered to be malarial in nature, but which, upon examination, turned out to be due to acute otitis media (in one instance due to the diplococcus lanceolatus).

The intermittent fever which is most commonly confused with malaria is that associated with *pulmonary tuberculosis*. It is probably no exaggeration to say that the majority of cases of pulmonary tuberculosis arising in the malarial districts of this country are, at some time in their course, mistaken for malarial fever. Intermittent fever, recurring often at fairly regular hours on succeeding days, is the rule at some stage, earlier or later, of pulmonary tuberculosis, while actual chills may occur. It is natural that the patient should ascribe such symptoms to malaria; there is, however, no excuse today for such error on the part of the physician. The sallow color, the anæmia, the enlarged spleen will serve to distinguish the malarial process from the tuberculosis, where, though the face be pale, the lips and mucous membranes show usually a good color, while splenic enlargement is rare. The examination of the lungs, sputa, and blood will determine the diagnosis.

The chills which often occur in the course of *gonorrhœa* or those following catheterization or the passing of sounds may be confused with malarial fever. The urethra should always be examined in doubtful cases. In some cases of grave septicæmia following gonorrhœa there may be little or no evidence of an actual urethritis. Here the examination of the blood will immediately settle the question. In the one instance there is leucocytosis without malarial parasites; in the other, a normal or reduced number of leucocytes with the presence of the malarial organism. In all these cases the final decision must be arrived at from an examination of the blood. It is through this alone that a positive diagnosis of malarial fever can be made.

Method of Examination of the Blood.—For the satisfactory examination of the blood an oil-immersion lens is absolutely necessary. No physician today can consider himself equipped for practice without a good microscope and an oil-immersion lens. Though much valuable work has been done with dry lenses and lower powers, it is folly to attempt careful work without better means. The simplest and best method of studying the malarial parasite is in the fresh blood at the bedside or in the consulting room. The steps toward the preparation of the specimen are quite simple, though certain precautions must be rigidly adhered to. The cover-glasses and the slides must be carefully washed in alcohol or alcohol and ether in order to remove all fatty substances; they should always be washed immediately before use. The blood may be taken from any part of the patient's body, though the lobe of the ear is perhaps preferable, inasmuch as it is less sensitive and more readily approached than the finger-tip, while a smaller puncture will draw more blood. This method is also more satisfactory than the puncture of the finger, in that the patient cannot so readily observe the proceeding—a point of considerable importance in nervous patients and in children. The ear is first thoroughly cleaned; the lobe is then punctured with a small knife or lancet. For the most careful procedures it is advisable to wash the ear with soap and water, and afterward with the alcohol and ether. But, practically, it is often advisable to make as few preparations as possible, and unless the ear or finger be extremely dirty one may proceed at once. A pin or needle will, of course, answer the purpose, but it is well to remember that a stab made by a round blunt-pointed instrument is much more painful than that by a sharp cutting edge, while a considerably deeper stab is required to draw a given quantity of blood. If a very sharp spear-pointed lancet be used, and the lobe of the ear taken firmly between the fingers so that the skin is held tense, very slight pressure with the tip of the lance will cause an incision deep enough for all purposes. This process is almost without pain to the patient. By proceeding carefully blood may often be obtained in this manner from a sleeping infant without its awakening.

After the first several drops of blood have been wiped away the freshly cleaned cover-glass is taken in a pair of forceps and allowed to touch the tip of a minute drop of blood. It is then placed immediately upon a perfectly clean slide. It is well, if a third person be present, to allow the slide to be vigorously rubbed with a clean linen cloth just before the application of the cover-glass. The spreading out of a drop of blood will be thus considerably facilitated. If the slide and cover be perfectly clean, the blood will immediately spread out between them, and, unless the drop of blood be too large, the corpuscles may be seen lying side by side entirely unaltered in their main characteristics. The drop of blood which is taken should be very small unless the patient be very anæmic, and care should also be exercised that the tip of the drop only touch the cover. If the cover be placed rudely against the drop and pressed perhaps also against the ear, the blood may so far spread out that the process of drying may have begun at the edge of the drop before the glass is laid upon the slide. If this be the case, the immediate spreading out of the blood between the slide and the cover does not occur. No pressure whatever should be exerted upon the cover, which should not be pushed or allowed to slide. The specimens will remain in good condition for a considerable length of time, an hour or more—long enough to be thoroughly examined. If one desire to observe the specimen for a greater length of time, the periphery of the glass may be surrounded by paraffin or vaseline. In this manner we may see the parasites living and in active motion, while the most exquisite examples of phagocytosis may be observed. By enclosing the specimen in paraffin or vaseline the preparations may, if handled carefully, be carried from the residence of the patient to the consulting room and there examined, but under these circumstances one must generally rely upon dried and stained specimens.

The preparation of specimens for staining is quite simple, requiring only a little experience and practice. Stained specimens are of especial assistance in the detection of the unpigmented hyaline bodies, particularly the pale tertian forms and those of the æstivo-autumnal parasites. A small drop of blood flowing from the lobe of the ear or the finger-tip is collected upon a perfectly clean cover-glass, which is immediately placed upon another glass. The drop of blood, if the two covers be perfectly clean, spreads out immediately between the glasses. The cover-glasses are then drawn apart. If neither glass be lifted or tilted during this process, they will slide apart readily without sticking. If the glasses have remained together so long that they have begun to adhere, one may be sure that the specimen will be no longer perfect. The glasses, thus prepared, are allowed to dry in the air, which they do usually in the course of a few seconds, and may then be preserved for an almost indefinite length of time. To prepare them for staining the glasses should be heated upon a copper bar or in a thermostat at a temperature of 100° to 120° C. for two hours, according to the method of Ehrlich, or they may be placed in absolute alcohol and ether, equal quantities, for two hours or more (Nikiforov's method).

The malarial parasite is readily stained by most of the basic nuclear dyes. The simplest method is perhaps to stain with a concentrated aqueous solution of methylene blue or *Löffler's methylene blue*:

Concentrated alcoholic solution of methylene blue,	30 c.c.
Solution of caustic potash 1 : 10,000	100 "

In either instance, the specimens should be stained for from thirty seconds to a minute, washed in water, dried between filter papers, and mounted in oil or balsam. The red corpuscles then will be unstained, while the nuclei of the leucocytes and parasites will be stained a clear blue.

A contrast stain may be obtained by the following method: The cover-glass specimen, after fixing in absolute alcohol and ether from four to twenty-four hours, is placed for a few seconds (thirty seconds to five minutes) in a 0.5 per cent. solution of eosin in 60 per cent. alcohol, washed in water, dried between filter papers, and placed for from thirty seconds to two minutes in a concentrated aqueous solution of methylene blue, or in Löffler's methylene blue, washed in water, dried between filter papers, and mounted in Canada balsam. The red corpuscles and the eosinophilic granules are stained by the eosin, while the nuclei of the leucocytes and the parasites take a blue color.

Admirable results may be obtained by a modification of *Romanovsky's* method. Two solutions are necessary—a saturated aqueous solution of methylene blue and a 1 per cent. watery solution of eosin. The older the methylene blue solution the better the results. The staining mixture should be made just before it is to be used. To one part of the filtered methylene blue solution about two parts of the eosin solution are added. This is carefully stirred with a glass rod and poured into a watch-glass; it should not be filtered after the mixture has been made. The cover-glasses, fixed according to the methods above described or by hardening in alcohol for from ten minutes upward, are allowed to float upon the top of this fluid. The specimens are covered by another inverted glass, and the whole by an inverted cylinder which is moistened on the inside. In from half an hour to three hours—best in two or three hours—good specimens are obtained.

For quick work in the consulting room the simple stain with methylene blue alone is perfectly satisfactory, though the observer must of course have sufficient experience to be able to distinguish precipitates which may be present in the staining solution from parasites.[1]

The discovery of malarial parasites in the red blood-corpuscles is, of course, a positive sign of the malarial nature of the process. In some instances where the parasites may be very scanty or absent the presence or absence of a leucocytosis is an important diagnostic sign. As will be remembered, the leucocytes in malarial fever are normal or diminished in number, whereas in almost all processes with which the acute intermittent malarial fever may be confounded there is a well marked leucocytosis. This is the case in all the septic infections which are most likely to be confounded with tertian and quartan fever; it is also true of tuberculosis, at least when accompanied by intermittent fever. The presence of a marked leucocytosis is strong presumptive evidence against the existence of malarial fever. In some instances where very few parasites are present the finding of pigment-bearing leucocytes may be an important aid in diagnosis. Tertian and quartan infections where multiple groups of parasites are present may occasionally be confounded with typhoid fever. Well marked remissions and, almost invariably, actual intermissions, usually occur, while the examination of the blood will readily clear up the diagnosis.

The differential diagnosis between tertian and quartan infections may be readily made in the fresh specimen, less distinctly in the stained. The larger and more actively amœboid, pale tertian parasite with fine brownish, actively dancing pigment granules may be readily distinguished from the smaller, less active, more refractive quartan parasite with its coarser, more slowly moving, darker granules. In the case of the tertian parasite the red corpuscles may be seen to become expanded and pale with the growth of the organism, while in the quartan parasite the corpuscle is shrunken and of a deeper, more brassy color. If the blood be examined just before or during the paroxysm, the more irregularly segmenting tertian organisms with their numerous (twelve to thirty) segments may be clearly distinguished from the smaller regular forms in quartan fever with their fewer (six to twelve) segments. The presence, in either instance, of one or more groups of parasites may usually be readily determined. Combined infections with quartan and tertian parasites—which, though very rare, do exist—may also be readily made out.

In the stained specimen the size of the pigment and the parasite

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[1] The experienced observer may obtain sufficiently good specimens for diagnosis in many instances by rapid heating of the cover-glass over the flame for a few minutes; the results, however, are uncertain.

and the behavior of the red corpuscle, pale in one instance, taking a deep eosin stain in the other, and the characteristics of the segmenting forms, should enable us also to make a differential diagnosis.

If it be impossible to make a microscopical examination of the blood, the therapeutic test is usually sufficient; thus, in the regularly intermittent fevers there is rarely any recurrence of the fever after forty-eight hours from the beginning of the administration of quinine. In the majority of instances of tertian infection in this climate all traces of fever disappear within twenty-four hours.

(2) THE ÆSTIVO-AUTUMNAL FEVERS.—While the diagnosis in the regularly intermittent tertian and quartan fevers is a relatively simple matter, the same is not true of the more irregular æstivo-autumnal forms of malaria. In some instances, where the paroxysms are of shorter duration and occur at regular intervals, usually quotidian, the diagnosis may be as self-evident as in the regularly intermittent fevers. The longer paroxysms, occurring at intervals of approximately forty-eight hours one from another, with their less rapid rise, but with a complete intermission between them, are also generally easily recognized when we take into consideration the anæmia, the enlarged spleen, and the herpes labialis which are so commonly present. When, however, from any of the various causes above mentioned the separate paroxysms become more or less complicated or merged one with another, so that at first but slight transient intermissions, then perhaps only irregular remissions, and finally a continued high fever, result, the diagnosis becomes often more difficult. Such a case often presents itself in the form termed by Baccelli "*subcontinua typhoidea.*" The general clinical appearances are so similar to those of *typhoid fever* that a distinction without examination of the blood may be quite impossible. In a certain number of instances vestiges of the paroxysms still may be made out, a well marked acme in the fever being reached at approximately the same hour at quotidian or tertian intervals, though in other instances all traces of the individual paroxysms may have disappeared. Sometimes the history of several sharply intermittent paroxysms in the beginning of the illness may lead us to a correct diagnosis. Again, the prodromal symptoms are much less frequent and severe, as a rule, in malaria than in typhoid. Herpes is common in æstivo-autumnal malaria, unusual in typhoid fever. Delirium may appear quite early in a malarial attack; it is rare during the first few days of a typhoid. Bronchitis is more common in typhoid than in continued malarial fever. Marked abdominal symptoms, though they may occur, are unusual in malaria; the rule in typhoid fever. Certain erythemata, and especially, urticaria, may be present in malarial fever, while the characteristic typhoid roseola does not occur. In both instances the spleen is usually enlarged. An important diagnostic sign is the anæmia which is almost invariably present if the malarial fever has lasted more than a few days, while in typhoid fever anæmia during the first two weeks is rare. Another important sign is the slight icteric hue which is usually present in malaria; rare in typhoid. Ehrlich's diazo reaction is unusual in the urine in malarial fever; it was found in but 6 per cent. of the cases classified by Hewetson and the author, while it is almost invariably present in typhoid.

Here, however, as in all other forms of malaria, the final decision is to be reached only by examination of the blood, where the small, amœboid, and ring-shaped, hyaline æstivo-autumnal parasites are to be found. If the process has lasted a week or more, the pigmented ovoid and crescentic bodies are also usually present. In rare instances quite severe febrile symptoms may be present, while the peripheral circulation may at times show but a small number of parasites. Here the discovery of pigment-bearing leucocytes may often be of assistance. The diminished number of leucocytes which one finds under these circumstances does not help us in the differential diagnosis from typhoid fever, where also the leucocytes are almost invariably subnormal in number. If the case occur in a neighborhood where it is impossible to obtain the aid of the microscope, the diagnosis may be definitely made by the therapeutic test. No malarial fever now known resists good doses of quinine for more than three or four days. It is generally safe to say that if the process be malarial the temperature will be practically normal by the fourth day. If quinine fails to influence the fever, we may rest assured that the process is either non-malarial or a mixed infection.

The confusion with typhus fever might occur in some instances, but here, again, the examination of the blood will settle the question.

As in the case of the regularly intermittent fevers, the process may be confounded with tuberculosis or other various septic infections. The one safe method of differential diagnosis is the examination of the blood.

PERNICIOUS MALARIA.—The diagnosis in some pernicious paroxysms may be at times confusing.

Comatose Pernicious Fever.—This type of fever must be distinguished from sunstroke, uræmia, cerebral hemorrhage. The differentiation of such an attack from sunstroke is by no means simple. As Bastianelli and Bignami have pointed out, individuals who are subjected to malarial infection are often those working in the fields and most exposed to the rays of the sun at the hottest season of the year, while the clinical symptoms of the two processes may be closely similar. It is interesting to note that the case of comatose pernicious fever referred to above as occurring in a tertian infection was at first mistaken for sunstroke. The slight jaundice, the anæmia, the enlarged spleen would serve to suggest the malarial nature of the process, while the examination of the blood gives a positive clue to the diagnosis. In the *tetanic, meningeal, eclamptic*, and *hemiplegic* types the same symptoms may lead to a correct diagnosis.

The Algid Type.—In this type of paroxysm, where the temperature may be normal or subnormal, and where often (from the actual condensation of the blood) the anæmia may not be as apparent, the diagnosis may be considerably in doubt. Here, however, icterus and enlarged spleen are suggestive, while examination of the blood will give positive diagnosis. It is in cases of this nature that the physician who makes systematic blood examinations in all doubtful cases will be enabled at times to gain information which will save the life of his patient.

The Hemorrhagic Type.—The diagnosis in some of the instances of this nature must be made between malarial and yellow fever. The early appearance of albumin and casts in yellow fever is suggestive, while the spleen is often but little enlarged in this affection.

The examination of the blood may in some cases be the sole reliable method of differentiation.

Malarial Hæmoglobinuria.—The diagnosis here lies usually between yellow fever, the ordinary paroxysmal hæmoglobinuria, and acute nephritis from some other toxic origin. And here, again, the chief reliance must be placed upon the examination of the blood.

Post-partum and Post-operative Malaria.—A diagnosis of these conditions can only be made upon examination of the blood. The malarial paroxysms differ from the paroxysm due to septic infection chiefly by their greater regularity and by their average longer duration. The blood, apart from the presence of the specific parasites and pigment, shows in the one instance diminution in the number of leucocytes, and in the other well marked leucocytosis.

Chronic Malarial Cachexia.—The diagnosis of chronic malarial cachexia is usually relatively easy. It is chiefly to be confounded with grave primary or secondary anæmia or with leukæmia and pseudoleukæmia. The malarial process may usually be distinguished from splenic anæmia by the presence of pigment and parasites in the blood. In some instances, however, where these are not to be found, the enlarged spleen, the grave anæmia, the hemorrhagic tendency, the dropsical effusions present in both conditions may render the diagnosis almost impossible without appealing to the history of the patient. The progress of such cases under proper treatment is usually, however, decisive. The malarial cachexia responds generally, slowly but progressively, to treatment. Thus, the author has seen a spleen which reached beyond the umbilicus and almost to the pubes diminish under treatment until it was only just palpable, while the blood returned from 1,000,000 red corpuscles to the cubic centimetre to the normal condition, the patient remaining in perfectly good health in a non-malarious district. The diagnosis from leukæmia is readily made by examination of the blood.

Post-malarial Anæmia.—An absolute differential diagnosis between post-malarial anæmia and some other secondary anæmiæ is impossible. The tendency, however, in the post-malarial anæmia to a diminution in the number of leucocytes is always marked, while a relative increase in the large mononuclear elements is very suggestive. As has been said before, there is nothing characteristic in the *nephritis* which follows malarial fever.

Other Complications and Mixed Infections.—In some of the mixed infections to which reference has been made above a certain diagnosis can only be made by the discovery of the parasites and the persistence of the complicating process after the disappearance of the organisms under quinine. Thus, the diagnosis of *typhoid fever* may be made if the characteristic symptoms continue after the clearing up of the complicating malarial process.

In the case of *pneumonia* the diagnosis depends more upon the physical examination, knowing as we do that the malarial parasite is of itself incapable of producing actual pneumonic consolidation. The same is true of *pleurisy.*

The occurrence of *diarrhœa* or *dysentery* during the active malarial process may or may not be directly due to the malarial poison. The presence of the Amœba coli in the stools is evidence of a complicating process, while in other instances of diarrhœa in acute malaria the result of the specific treatment must be awaited before one can form a definite diagnosis.

Parotitis, tonsillitis, acute rheumatism, the *exanthemata,* occurring in connection with malarial fever, may be recognized by their usual symptoms.

PROGNOSIS.

The Regularly Intermittent Fevers.—The prognosis in tertian and quartan fevers as for ultimate recovery is almost invariably good. The writer knows of but one instance in which actual pernicious symptoms were present in tertian or quartan infection. Without systematic and careful treatment relapses and grave cachexia may, however, follow—a cachexia which may well lay the patient open to the gravest secondary complicating processes. It is not improbable that in certain of these instances a fatal chronic nephritis may follow repeated malarial infections.

Æstivo-autumnal Fever.—In ordinary cases of æstivo-autumnal fever which come early under treatment the prognosis is perfectly good. Treatment must, however, be more active and longer carried out than in the regularly intermittent fevers. Imperfectly treated cases are more likely to be followed by cachexia and grave post-malarial anæmia.

Pernicious Fevers.—Wherever pernicious symptoms have developed the prognosis is extremely grave, and, unless active treatment be instituted, usually wholly unfavorable. In a patient first coming under observation in a pernicious paroxysm an entirely favorable prognosis can never be given for at least forty-eight hours after the beginning of treatment. It is always possible that a single pernicious paroxysm may be succeeded, despite treatment, by another upon the following day. If active treatment has been begun during a pernicious paroxysm and no succeeding paroxysm has occurred within forty-eight hours, the prognosis is usually favorable.

Malarial Hæmoglobinuria.—The prognosis here is always extremely grave; indeed, the dangers of a fatal outcome are not past until several days after the complete disappearance of fever and of symptoms on the part of the urine.

Chronic Malarial Cachexia.—In the milder grades of chronic malarial cachexia the prognosis is good if the patient can be compelled to adopt a properly hygienic life. In the more severe grades recovery is extremely slow, and at times almost impossible, unless the patient be transferred into a more healthy region.

Post-malarial Anæmia.—The anæmiæ following malaria are often extremely grave. In those instances where the nucleated red corpuscles are scanty or absent and the leucocytes are diminished in number, and in those cases where the blood shows the characteristics of true pernicious anæmia, the prognosis is extremely grave.

The prognosis in the various *complications* of malaria is influenced only by the possible unfavorable effect of the coexisting malarial infection. Secondary infections occurring in individuals suffering from malarial cachexia appear to pursue an unusually unfavorable course.

TREATMENT.

GENERAL MEASURES.—Certain general hygienic measures are advisable, and sometimes very important, in the treatment of malarial fever.

Rest in Bed.—It is always prudent, if possible, to keep a patient with malarial fever in bed for twenty-four or forty-eight hours; in the more severe æstivo-autumnal fevers it is absolutely necessary. The simpler regularly intermittent fevers often show a temporary and sometimes permanent spontaneous recovery following rest in bed, without further treatment. In hospital practice it is our rule to keep a patient with malaria in bed until the entire disappearance of fever, whether it be intermittent or subcontinuous. It is not impossible that the more satisfactory results of hospital treatment may, in part, depend upon the fact that the patients are so much more readily kept at rest.

Change of Surroundings.—If the patient's dwelling be in a malarious district, it is always important, if possible, that the individual be removed into more healthy surroundings. Thus, recovery from chronic cachexia is greatly favored by the removal into higher, more healthy regions. In some instances of advanced cachexia the removal may be absolutely necessary. In the ordinary acute malarial fevers it is, however, generally perfectly possible to treat the case in the malarial district itself. The patient should be kept, while under treatment, in one of the upper stories of the house; he should be warned against remaining out of doors at night during convalescence, and prevented, as far as possible, from subsequent exposure to infection.

Diet.—In the simple intermittent fevers the patient may be given an ordinary nourishing general diet. During the paroxysms, which last but ten or twelve hours in all, the patient need not be forced to eat; it is, however, generally well that liquids, milk, broths, soups, should be taken in small quantities. Stimulants may be administered symptomatically. In the more severe subcontinuous fevers, where there is usually complete anorexia, the patient may be given liquids of all sorts, soups, milk, broths, at short intervals; while, if he be hungry and there be no gastro-intestinal symptoms, there is no contraindication to soft solids and eggs. In cases where there are marked gastro-intestinal symptoms great care must, of course, be exercised with the diet. Easily digested liquids, such as boiled milk, albumin-water, and broths should alone be given.

Exposure to the Air.—There are districts where experience has led the inhabitants to believe, probably justly, that exposure to the night air is injudicious. It may be unwise in such regions for the patient to be allowed to sleep with his window open. If, however, the patient be in a healthy district and be accustomed to living and sleeping with open windows, there is no reason why a change should be made during the existence of the fever. There is no fever which we know today which is unfavorably influenced by fresh air and open windows, provided the individual be accustomed to such air beforehand.

QUININE.—Malarial fever is one of the few diseases against which we possess a remedy which truly deserves to be called specific. This remedy, in the form of cinchona bark, was introduced into Europe in 1640 by the countess del Chinchon (wife of del Chinchon, the Spanish governor of Peru), who had recovered from a severe attack of intermittent fever after taking a powder administered by a *corregidor* of Loxa. As far as is known, this substance was first used by the Indians in this region as a remedy against malarial fever. The powder, which was known at first as "the powder of the countess," and afterward as "the Jesuits' powder" for the reason that it was introduced into general use by the Jesuits in Rome in 1649, was prepared from the bark of a Peruvian tree. This was for years known as Peruvian bark, though its officinal name, Cinchona, is derived from that of its introducer to the Eastern hemisphere. It was at first administered in the form of the pulverized bark, the cinchona powder, which contains, in addition to various alkaloidal substances, a considerable quantity of tannin. Today, however, the pulverized bark is no longer in general use, its place having been taken by various salts of its active principle, quinine.

Action of Quinine on the Malarial Parasite.—For centuries after the introduction of quinine and after its specific action in malarial fever had been noted the exact mode of action remained unknown. As long ago as 1867, Binz[1] correctly concluded that the efficacy of quinine in paludism depended upon its action as a protoplasmic poison upon some lower organism which he assumed to be the cause of the process. The extremely toxic action of quinine upon the infusoria was at that time clearly demonstrated. Since the development of our knowledge concerning the malarial parasite it has been possible to study, to a certain extent, the direct action of quinine upon the hæmatozoa. Laveran noted the immediate disappearance of the parasites following the administration of quinine, and in 1881 asserted that "it is because it destroys the parasite that quinine causes the disappearance of the manifestations of paludism." He showed that by allowing a 1 : 10,000 solution of quinine to run under the cover-glass the movements of the parasite were immediately arrested, as they are upon subjecting the organism to any other protoplasmic poison.

Golgi[2] has studied the action of quinine on the tertian and quartan parasites. He noted that after the administration of quinine the quartan organism, in its endoglobular stage, shows a coarser granulation with a metallic reflex, while the protoplasm shows a certain cloudiness. At times one may see abortive segmenting forms which are smaller than the normal, with a lack of regularity and fewer segments. The pigment also may not collect as sharply in a clump in the middle of the parasite. In the tertian parasite the changes are more marked, owing to the greater normal activity of the organism. The body is round and immovable, and shows a sharper outline than usual, while the pigment has a peculiar metallic reflex and tends to collect in clumps. Full grown tertian forms may present a large transparent swollen condition with very active movements of the pigment granules. Sometimes the pigment may collect toward the periphery, leaving an hyaline space in the middle. Mannaberg[3] asserts that three hours after the administration of 0.5 of quinine the amœboid forms of the tertian parasite show a marked diminution in their activity. In several hours more the number has greatly diminished, while many of those present are fragmented, resulting in the presence of several separate spherules in the red corpuscle. Full grown forms show a cessation of the movements of the pigment, the body having a somewhat refractive homogeneous appearance. Large hydropic forms with active pigment may also be seen. These two latter forms may occur normally during the paroxysm, as Golgi and Mannaberg also assert; they are probably degenerate forms. The writer has also observed in the case of the tertian parasite the somewhat greater refractiveness of the organism, the collection of the pigment into clumps, and the cessation of active movements, as well as the presence of a greater number of fragmenting forms

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[1] *Centralblatt f. d. med. Wiss.*, 1867, p. 308.

[2] *Deutsch. med. Woch.*, 1892, 661, 695, 707, 729.

[3] *Loc. cit.*

Romanovsky[1] and Mannaberg[2] have made interesting studies with stained specimens. Both observers note the loss of affinity for coloring matters in the chromatin substance of the nucleus. They also note that in the segmenting forms, after quinine has been given, the greater number of the segments show no nucleoli. These changes in the nucleus they believe to be evidence of a necrotic process. The segments without nucleus Mannaberg terms "still-born." Baccelli[3] noted that in æstivo-autumnal fever after the intravenous injection of quinine there was an increase in the activity of the small amœboid forms, which, often inside of twenty-four hours, disappeared without showing any outward signs of degeneration. Marchiafava and Bignami,[4] studying the æstivo-autumnal fevers, note that the administration of quinine is followed by an increase in number of shrunken, brassy colored corpuscles. They believe that the included parasites are incapable of further development.

Most observers who have been able to test the action of quinine upon the malarial parasite will agree with Golgi that in tertian and quartan fever quinine acts most markedly on the free young segments, less upon the more advanced forms where the red corpuscle is in greater part destroyed, and least upon the young endoglobular forms. If quinine be given several hours before the paroxysm, it will not prevent segmentation, but it will destroy the new group of parasites, the fresh segments. Segmentation takes place, toxic substances are produced and enter into the blood serum, and the chill follows, being at most a little modified or retarded. The further development of the new group of organisms is, however, prevented, and on the following day no parasites whatever may be observed. Marchiafava and Bignami[5] arrive at the same conclusion in the case of the æstivo-autumnal parasite. They state "that the maximum and most rapid action of the remedy is exercised on that phase of the extraglobular life of the parasite which follows the completed segmentation." They note, as does Golgi in the case of the tertian and quartan organisms, that the segmentation cannot be prevented if quinine be given when the parasite has reached the preparatory stages. "Quinine," they say, "acts on the amœba of malaria during those phases of its life in which it absorbs nourishment and develops; when the nutritive activity comes to an end, the transformation of hæmoglobin into black pigment having been accomplished, and the phase of reproduction begins, then quinine becomes inefficacious against this process."

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[1] *Cent. für Backt.*, 1892, xi. Nos. 6 and 7, 219; and *St. Pet. med. Woch.*, 1891, Nos. 34 and 35.

[2] *Loc. cit.*, and *Cent. für klin. Med*, 1891, No. 27.

[3] *Deutsch. med. Woch.*, 1892, No. 32, 721.

[4] *Loc. cit.*

[5] *Loc. cit.*

To best combat the further development of a group of malarial parasites quinine should be in solution in the blood at the time of the setting free of the fresh parasites—*i. e.* during and several hours before the paroxysm. In ordinary tertian or quartan fevers, with moderate regular daily doses of quinine, the parasites will usually wholly disappear from the peripheral circulation inside of three days. In æstivo-autumnal fever the time may be a little longer. All observers agree that the crescentic bodies are affected slowly if at all by quinine; they remain in the blood long after all other forms of the parasite have disappeared.

Effects of Quinine upon the Human Being.—In small doses, such as are ordinarily required therapeutically, quinine causes no subjective symptoms. In somewhat larger doses, however, it produces at times a ringing in the ears, roaring or sometimes tinkling noises, and, finally, more or less deafness. Larger doses are followed by a dimming of the vision, even to complete blindness. Ringer has noted that this may sometimes begin in one eye, and, indeed, exist for considerable time upon one side alone. The pupil is usually dilated. In larger doses a severe frontal headache, with giddiness and staggering gait, delirium, and great muscular weakness, may follow, and, finally, in still larger doses, convulsions and death. At times large doses of quinine are followed by certain cutaneous disturbances. Ringer describes an intense general erythema similar to a scarlet fever rash and followed also by desquamation. Urticaria also at times occurs.

Manner in which Quinine should be Given.—Like another commonly used and extremely valuable drug, digitalis, quinine, which is our main stay in malarial processes, is very frequently abused. Laveran well says: "In a general way it may be said that in malarial districts far too much sulphate of quinine is given to patients who have no need of it, while a sufficient quantity is not given to patients suffering from paludism." The very degree of its efficacy, as in the case of mercury and iodide of potassium in syphilis, is probably accountable for the lax manner in which it is frequently given. When one or two doses are followed by a complete disappearance of symptoms, the immediate relief is so great that the patient fails to recognize the importance of continued treatment, and, by abandoning the regular régime, lays himself open to repeated relapses.

It is of considerable importance to determine in an individual case how and in what form quinine should be given. The following tables, taken from Laveran, show the percentage of quinine which the different salts contain, as well as their relative solubility:

Salts of Quinine classified according to the Percentage of the Alkaloid which they contain.

	Quinine.
100 parts of the basic muriate of quinine contain	81.71 per cent.
" " neutral " " "	81.61 "
" " basic lactate " "	78.26 "
" " " hydrobromate " "	76.60 "
" " " sulphate " "	74.31 "
" " " sulphovinate " "	72.16 "
" " neutral lactate " "	62.30 "
" " " hydrobromate " "	60.67 "
" " " sulphate " "	59.12 "
" " " sulphovinate " "	56.25 "

Salts of Quinine classified according to their Solubility in Water (Regnauld and Villejean).

					Water.
1 part	of the	neutral	hydrochlorate	of quinine is soluble in	0.96
"	"	"	sulphovinate	" " "	0.70
"	"	"	lactate	" " "	2.
"	"	basic	sulphovinate	" " "	3.30
"	"	neutral	hydrobromate	" " "	6.33
"	"	"	sulphate	" " "	9.00
"	"	basic	lactate	" " "	10.29
"	"	"	hydrochlorate	" " "	21.40
"	"	"	hydrobromate	" " "	45.02
"	"	"	sulphate	" " "	581.00

The ordinary method of administering quinine is by the mouth; the common form in which it is given in this and most countries is as the *sulphate.* The *sulphate of quinine* is very slightly soluble in water, but quite readily soluble in dilute acids. The best manner to administer this form of quinine is in water containing a sufficient quantity of dilute hydrochloric or sulphuric acid to hold the salt in solution.[1] The extremely bitter taste is sometimes an objection in sensitive patients: this, in the case of the quinine powder, may be partly obviated by mixing with an equal quantity of powdered ginger. The drug may also be administered in the form of pills or in capsules. Quinine pills are convenient, but are open to the common objection that in many instances the commercial pill is an highly insoluble object. Thus, it is not at all infrequent in dispensary practice for the physician to be consulted by patients with simple intermittent fever who have taken quinine pills[2] without effect, while the solution or the powder has an immediate result. For more rapid action the quinine may be administered hypodermically or, according to the method of Baccelli, intravenously. For these purposes more soluble salts than the sulphate must be used. Thus, for subcutaneous use the *neutral hydrochlorate of quinine* is an excellent salt. De Beurmann and Villejean[3] use the following formula:

℞. Bihydrochlorate of quinine,	5.
Distilled water,	q.s. ad 10.

1 c.c. (♏xv) of this solution contains 0.5 (gr. vijss) quinine.

If the hydrochlorate of quinine is not to be obtained, one may make use of the ordinary sulphate, as follows:

℞. Sulphate of quinine,	1.
Tartaric acid,	0.5
Distilled water,	10.

The officinal *bisulphate of quinine* is soluble in about 9 or 10 parts of water, and may be used hypodermically if a more soluble salt cannot be obtained.

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[1] The druggist customarily adds about 1 drop of the dilute acid to 1 grain (0.65) of the salt.

[2] My colleague, Dr. L. F. Barker, has actually observed the discharge of well preserved quinine pills from fæcal fistulæ in three instances.

[3] Quoted from Laveran, *Du Paludisme, etc.*

Baccelli[1] uses, as an intravenous injection, the following mixture, which he has found to act with the greatest rapidity and the most marked effect:

℞. Quininæ hydrochloratis,	1.0
Sodii chloridi,	0.075
Aquæ destillatæ,	10.0

The solution is perfectly clear and should be injected lukewarm. The procedure is described by Baccelli as follows: "After the veins of the forearm have been made turgescent by means of a circular tourniquet above the elbow, we introduce a Pravaz needle in a direction from below upward into the lumen of the vein. We select a small one in order to avoid hemorrhage afterward. Generally, we are accustomed to select one situated upon the flexor side of the forearm. The syringe holds 5 c.c., and is filled according to the dose which is to be given, and connected with the needle before its introduction." The most rigid antisepsis must be observed. The stab wound is closed with collodion after the needle has been withdrawn.

The *bimuriate of quinine and urea*, which contains nearly 80 per cent. of quinine and is soluble in less than its own bulk of water, is another convenient form in which to administer the drug.

The hypodermic use of quinine is attended by considerable pain and real danger of a subsequent abscess or necrosis. If the solution and the instruments be carefully sterilized, there is little danger of abscess, but at times a considerable area of necrosis may result. It is always important to introduce the needle well into the subcutaneous tissue; if this be neglected and the solution be introduced into the deeper part of the cutis, necrosis usually follows. Quinine may be given by rectum; this is, however, a last resort, and is practically never necessary excepting, at times, in children.

The Time at which Quinine should be Given.—If one but remember the studies of Laveran, Golgi, Mannaberg, and others concerning the effect of quinine upon the parasite, and then consider the close relation between the development of the parasite and the symptoms of the malarial infection, one may readily perceive the time at which, theoretically, the drug should be best administered. Inasmuch as it has been shown that quinine acts most effectually upon the young extracorpuscular parasite, it would seem fair to conclude that the period just before or during the paroxysm should be that at which quinine might be administered with most effect, and, as has been clearly shown, this is the case. A dose of quinine shortly before a paroxysm in the regularly intermittent fevers will not affect that paroxysm, but will prevent a recurrence of the succeeding one dependent upon that group of organisms. Thus, a single moderate dose of quinine given just before or during a paroxysm in single tertian or quartan infection will cause generally a total disappearance of the symptoms, while in the case of a double tertian infection it may often be seen to change the type of the fever from quotidian to tertian. Thus, in such an instance the paroxysm expected upon the following day will occur, but that expected in forty-eight hours will not appear, the greater part of the group of parasites having been destroyed. The same has been shown to be true in æstivo-autumnal fever, though the parasites are much more resistant to the action of quinine than those of the regularly intermittent fevers.

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[1] *Studien über Malaria*, Berlin, 1895.

Administration of Quinine in the Regularly Intermittent Fevers.—Here it is generally best to place the patient upon regular continued treatment with quinine. If it be possible to keep the patient in bed, very small doses will often be sufficient. Thus, 0.065 (gr. j) three times a day will, in many instances, be followed by a disappearance of the symptoms. In practice we may give, according to the severity of the case, from 0.13 to 0.325 (gr. ij–gr. v) three times a day. If in tertian fever the patient be seen on the day between the paroxysms, 0.325 (gr. v), three times a day will generally, if the patient be confined to bed, prevent even any succeeding paroxysm. One may predict, almost with certainty, the entire disappearance of the fever after this. If the patient be seen first just before an expected paroxysm or during the attack, it may be well to give a single large dose, 0.325–0.65 (gr. v–gr. x), and follow this by smaller doses, 0.13 (gr. ij), three times a day. If the paroxysms have been severe, it is sometimes wise to give large doses of the drug (0.325–0.65 (gr. v–gr. x)) during the first days of treatment at the hour when without treatment the paroxysm might have been expected. The parasites in tertian and quartan infections disappear from the blood generally within three days, but treatment with small doses, 0.4 (gr. vj), in twenty-four hours should be continued for at least three weeks.

Æstivo-autumnal Fevers.—In the treatment of æstivo-autumnal fever larger quantities of quinine must, as a rule, be given. In ordinary cases where no pernicious symptoms have developed one may start treatment with 0.325 (gr. v) every four hours. In most cases under such treatment fever will entirely disappear inside of three days. If symptoms of cinchonism develop, the dose may be reduced. If the patient come under observation during a paroxysm, or if the history be obtained of a severe paroxysm having recently occurred, it may be well to begin with larger single doses. Thus, during or just before a paroxysm 0.65 (gr. x) may be administered, followed by 0.325 (gr. v) every four hours. If severe nervous manifestations accompany the paroxysm and the development of pernicious symptoms be feared, it may be well to administer the quinine hypodermically or intravenously. It is rarely necessary to give doses larger than 1.0 (gr. xv). It may rarely be necessary to give several doses of this size at intervals of several hours during a long-continued paroxysm; usually two or three doses at intervals of four hours are sufficient, while afterward it will be possible to give smaller quantities (0.325) every four hours. Such doses will usually prevent the recurrence of a paroxysm due to this group of parasites. It is, however, possible that a second large group of parasites, which all treatment has failed to influence, may on the following day produce a fatal paroxysm. The same course should be pursued during the succeeding paroxysm. It has long been a well recognized fact in malarious districts that if the patient survive the second paroxysm after the beginning of treatment, ultimate recovery is usually assured. In true *pernicious* paroxysms the experience of Baccelli would seem to show that intravenous injections of quinine are by far the most efficacious.

Baccelli has used successfully the solution of quinine described on page 150. It is apparently unnecessary to use doses larger than 1.0 (gr. xv).

Malarial Hæmoglobinuria.—The same general rules which apply to the treatment of the other pernicious fevers hold good in the case of malarial hæmoglobinuria. It should, however, be noted that certain observers believe that large doses of quinine exert a distinctly injurious influence upon the blood, aggravating often the destruction of the red corpuscles. Thus, Plehn[1] in a recent article goes so far as to advise an expectant treatment in these cases, asserting that recovery is more likely to result under careful nursing and general treatment than under the administration of quinine. This view is not held by the majority of observers.

CINCHONISM.—*Contraindications to Quinine.*—There is a great difference in the susceptibility of different individuals to quinine. Relatively small doses produce cinchonism in some individuals, while others are extremely tolerant of the drug. In the majority of instances, however, in which complaint is made it is based upon the fact that the drug has been administered in injudiciously large doses. The writer has never observed but one case in which it was impossible to administer quinine in sufficient doses to combat ordinary malarial manifestations without serious symptoms. In this instance, occurring in a colleague, the symptoms produced by quinine or other cinchona derivatives are interesting enough to mention here. After taking 0.13 (gr. ij) of the sulphate of quinine, in half an hour the patient had a feeling of oppression in the epigastrium, followed by nausea, vomiting, and then soon by "a hot prickling sensation over the entire skin." On one occasion, without extreme itching, there was an intense scarlatinoid erythema, lasting for hours and followed by desquamation; on another occasion, after 0.195 (gr. iij) of salicylate of cinchonidia, a most intense general urticaria. Cases of this nature are extremely rare, and there are few instances probably in which individual susceptibility is any true contraindication to the administration of quinine in malarial fever. The prejudice against the drug is very strong in the mind of some individuals, and it is not infrequently wise for the physician to introduce quinine in a form unfamiliar to the patient.

OTHER CINCHONA DERIVATIVES.—Various other cinchona derivatives have been used as substitutes for quinine in the treatment of malarial fever. Thus, *cinchonin*, *cinchonidin*, *quinidin*, and *quinoidin* have been recommended. The efficacy of these drugs is, however, so far below that of the various salts of quinine that their employment is inadvisable.

METHYLENE BLUE.—Next to quinine, the most valuable remedy in malarial fever is, probably, methylene blue. This substance was first employed in 1891 by Gutmann and Ehrlich,[2] who were led to its use by the observation of Celli and Guarnieri that the malarial parasites were stained while yet living by this substance. They found that in small doses quite a marked effect was obtained in several cases of intermittent fever. Since this time the drug has been used by a number of different observers, most of whom agree in the conclusion that methylene blue possesses a well marked antimalarial action, the parasites often disappearing from the blood and the patient recovering after its administration. As an antimalarial agent it is, however, as the observations of the author[1] have shown, far below quinine in efficiency, while the parasite acquires, apparently, a certain tolerance to the drug after its continued use. In certain mild cases of the regularly intermittent fevers it may be given in doses of 0.13 every four hours in capsule, with possibly a curative effect. Larger doses have been given without ill effect—doses as high as 3.0 (gr. xlv) in twenty-four hours. The only unpleasant symptom following its use is, apparently, strangury, which may be prevented by the administration of small quantities of powdered nutmeg at the same time. After ingestion of methylene blue the urine has a deep blue color; the fæces become blue on exposure to the air. While in certain instances methylene blue may have a curative effect, it is so far inferior to quinine that its value is certainly extremely limited.

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[1] *Loc. cit.*

[2] *Berliner klin. Woch.*, 1891.

PHENOCOLL.—Within the last few years several Italian observers have reported moderate successes from the treatment of malarial fever with the hydrochlorate or acetate of phenocoll, a derivative of phenacetin. It may be given in doses of 1.0 (gr. xv). It has been prescribed in the treatment of malaria in children.

OTHER REMEDIES.—A large number of other drugs have been at one time and another employed in the treatment of paludism. Thus iodine, strychnine, sulphur, arsenic, alum, preparations of eucalyptus and helianthus have been recommended. With the exception of arsenic, which, as will be said, is often of use in anæmia and chronic cachexia, the value of these substances is slight.

FURTHER TREATMENT.—Besides the treatment with the specific drug, certain accessory and symptomatic measures are often important. The value of purgation has long been insisted upon, and the old custom of beginning the treatment of malarial fever by administering a mercurial purge is probably in some instances of value. In cases where there are grave intestinal symptoms it should be avoided. Profuse *vomiting* or *purging* during a paroxysm should be controlled, as far as possible, by morphia administered hypodermically. Excitement and active *delirium* during the fever may also at times require the use of morphia. In the *collapse* in pernicious fevers most active stimulation must at times be resorted to; alcohol, strychnia, and ether may be freely administered hypodermically. In the algid forms external heat should be applied, as well as enemata of warm water. In *continued high fever*, particularly if there be delirium, cold sponging or the actual cold bath may be of value.

During convalescence the most serious symptom with which we have to deal is the *anæmia*. In these cases iron and arsenic are our mainstays. In most instances iron alone, either in the form of Blaud's pills or as the tincture of the chloride, in full doses, will be followed by good results. In severe cases *arsenic* may be resorted to; it is best given in Fowler's solution (liquor potassii arsenitis). It is well to begin with small doses (gtt. iii, *t. i. d.*), and to increase the dose steadily, one drop every other day, until the physiological effect is observable—slight suffusion and injection of the conjunctivæ, gastro-intestinal symptoms. The dose should then, after a few days' pause, be reduced and maintained at the highest possible limit. Some very grave anæmiæ which closely simulate true pernicious anæmia and react but little to iron may show marked improvement after vigorous treatment with arsenic. It should be borne in mind that in rare cases arsenical neuritis may follow. In some instances it is well to continue the use of strychnia in some form as a bitter tonic during convalescence.

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[1] *Johns Hopkins Hosp. Bulletin*, 1892, No. 22, 49.

TREATMENT OF CHRONIC MALARIAL CACHEXIA.—The treatment of chronic cachexia is often a very difficult matter. Active treatment by quinine will readily remove the parasite from the circulation and put an end to acute symptoms, but the extreme debility and the grave anæmia are often very obstinate. Owing to the great susceptibility of such patients to fresh infections or to a reappearance of an old infection after the cessation of treatment by quinine, it is sometimes almost necessary to remove the sufferer to a non-malarious district. The anæmia, which is usually the gravest symptom, should be treated according to the suggestions given above. It is in these cases that persistent and vigorous treatment by arsenic is especially valuable. The patient should be kept from all undue exertion; if the anæmia be very grave, rest in bed is important. The diet should be most nourishing, and the patient should be allowed to sit in the sun and fresh air in the middle of the day if the climate be not too hot. Bitter tonics are often valuable, particularly strychnia. Most cases of this nature will recover, even in a malarious district, if treatment be properly carried out. The majority of cases of malarial cachexia owe their origin to the carelessness of the patient, who does not carry out proper treatment with quinine and fails to observe the ordinary prophylactic measures.

PROPHYLAXIS.—General public prophylactic measures, such as proper drainage, cultivation of the soil, and so forth, cannot be considered here. The individual, however, may adopt certain measures which may protect him in the most malarious districts. If it be necessary to visit, temporarily, notoriously malarious districts, let him, so far as possible, choose the season at which the fevers are least prevalent. The dwelling should be sought upon ground as high and dry as possible. Exposure at night in damp or marshy districts should be avoided; the sleeping apartment should be an upper story of the house. Despite the experimental evidence against the idea that infection occurs through the gastro-intestinal tract, it is prudent to boil all drinking water coming from malarious districts. Medicinally, quinine in small doses will often prevent infection. If the district be extremely malarious, the various simple wines containing cinchona are insufficient protection, and it is prudent to take several grains of quinine daily. Monti[1] has recently reported good results from the administration of the sulphate of quinine in doses of 0.40 (gr. vj) every other day. Sezary[2] believed that a smaller quantity, 0.15 (a little over gr. ij), daily was sufficient to protect the individual under most circumstances.

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[1] *Loc. cit.*

[2] *Médecine moderne*, 1892.

DENGUE.

BY HAMILTON A. WEST, M.D.

DEFINITION.—Dengue, Break-bone Fever, Knockel Koorts, Rheumatic Scarlatina, Eruptive Rheumatic Fever, are the principal names applied to an acute, benignant, specific fever of short duration, prevalent usually in extensive epidemics in tropical and subtropical regions. It consists of two paroxysms of fever separated by an interval either of complete apyrexia or a decided remission of temperature, and attended by severe muscular and articular pains, and, in a considerable proportion of cases, also by an eruption of variable character.

HISTORY.—Dengue first attracted attention by the extensive prevalence of an epidemic in the West India Islands in 1827; previously, in 1779, an account of its occurrence in Java was given by David Brylon, and in the subsequent year Benjamin Rush described an epidemic prevalent in Philadelphia. The West India epidemic began in September, 1827, in the island of Saint Thomas, rapidly extending southward over the Caribbean Islands to Colombia, and northward to various cities in the United States, notably Pensacola, Charleston, Mobile, New Orleans, and Savannah, a few cases occurring as far north as Boston, Philadelphia, and New York. The next extensive epidemic took place from 1848–50 in various large cities in South Carolina, Georgia, Alabama, Louisiana, and Texas. Reliable observers state that as many as eight-tenths of the population of such cities as Augusta and Charleston would have the disease during a period of six weeks, showing such rapid and general dispersion as hardly to be equalled in this regard by any other malady.

After about two decades dengue appeared in Arabia in 1871, extending southward by the routes of travel to Zanzibar and other towns on the East African coast; thence to Java, reaching and spreading over India in 1872, invading several English stations in China and Burmah, and extending to the Gulf States in 1873. This epidemic was not only widespread, but intense, in some places hardly a person escaping. In Madras it is said that every house was invaded. In 1880 another epidemic occurred, beginning in Cairo and spreading over the whole of Egypt, and extending afterward to many towns in North and South Carolina, Georgia, Florida, Mississippi, Louisiana, and Texas.

In 1883 an epidemic of dengue appeared in Syria, first observed at Latakia on the northern coast. It spread by importation, but never reached beyond two thousand feet above the level of the sea, the high and dry mountain air seeming to be unfavorable to its propagation. Its prevalence in Beyrout was almost universal. This epidemic prevailed in Egypt also, and was marked by the same characteristics of pandemicity. In 1885 there was a severe epidemic in the State of Texas, visiting many of the larger towns, not confined to those upon the Gulf Coast, as Galveston and Houston, but extending far into the interior, to San Antonio, Austin, Dallas, as well as to many smaller places, reaching an altitude of nine hundred feet above the sea level, and attacking a large proportion of the population in the infected localities. So far, with exception of the southern provinces of Spain, Europe has escaped. Dengue occasionally occurs sporadically in the places most subject to it, as in India, Northern Egypt, and various localities in the Gulf States. In Galveston sporadic cases or mild epidemics are not infrequent.

ETIOLOGY.—*Climate.*—It will be observed from the above imperfect historical sketch that the disease is restricted to quite definite territorial limits, its latitudinal range extending from about 32° N. to 22° S., and, though in rare instances it may have occurred as far north as Boston, New York, and Philadelphia, such events are exceptional.

Season.—The influence of heat as a predisposing factor is shown not only by the above facts, but by the occurrence of the disease in colder climates during the summer and autumn seasons, and its prompt disappearance upon the advent of winter. In strictly tropical climates, as in the West India Islands, it may prevail every month during the year, and does not seem to be affected by weather changes. In semi-tropical regions its extension into the winter months is apparently favored by an unusual prolongation of summer heat. In December, 1894, sporadic cases occurred in Galveston, as the month was unusually warm, reaching within two degrees of the highest mean temperature for twenty years. The question arises as to what influence high temperatures may have in the development of dengue. That no extraordinary range of temperature occurred during the years of most extensive epidemics in Texas is shown by the following: In August, 1873, the average temperature for the month was normal; September, 1° above; October, 2° below; November, 2° below; December, 1° below. In 1885, August, 1° above; September, 1° below; October, 2½° below; November, 1° above; December, normal.

A humid atmosphere appears generally to be favorable to the propagation of dengue fever, as will be noted by this condition prevailing in the localities where it has occurred with the greatest frequency. Such local influences are, however, not essential, as has been repeatedly shown by the occurrence of epidemics at altitudes of from six hundred to nine hundred feet above the sea level and in climates ordinarily dry and salubrious.

Influence of Race, Sex, and Social Condition.—The susceptibility to this disease appears to be almost universal. During the time of its epidemic prevalence it attacks with peculiar impartiality all ages and all classes of the population. There is hardly any infection, if we except epidemic influenza, which is so indiscriminate, so general, and so rapid in its march and progress.

Specific Causes.—Although the clinical history of dengue, and its apparent spread by air currents, individual contact, and fomites, point to a specific pathogenic micro-organism as its essential cause, no effort, so far as the writer knows, was made looking to the discovery of such causative agent until 1885. At this time, during the prevalence of an epidemic in Austin, Texas, Dr. J. W. McLaughlin made a series of observations by which he was finally convinced that he had isolated the micrococcus of dengue. The results of these investigations were reported to the American Medical Association at its meeting in 1886, were afterward briefly referred to at the International Medical Congress in 1887, and photographs of pure cultures were exhibited at the Pan-American Medical Congress in 1893. Dr. McLaughlin states: "1. That he examined microscopically the blood of twenty persons suffering from dengue in its various stages, taking it directly from the veins, and found in all a peculiar staphylococcus. 2. Using necessary precautions to exclude alien germs and obtain chemical cleanliness, he introduced upon the point of a sterilized platinum wire a small fraction of a drop of dengue blood into test-tubes containing sterilized culture jelly, and grew upon it the same micro-organisms which the blood contained. 3. Using requisite precautions against the introduction of any foreign element, he aspirated into a series of Liebig's potash bulbs the blood directly from the arm of a dengue patient. The bulbs were then hermetically sealed, and those micro-organisms which the blood contained allowed to grow upon the contents of the bulbs as a nutritive medium. The temperature was constantly maintained at 100° F. At the expiration of six months the contents of the first bulb was examined under high power, with the result of finding the same micro-organism as was present in the blood drawn directly from the arm of the fever patient and that had been grown pure on the culture media." Dr. McLaughlin thus summarizes the results obtained from the preceding methods of examination: "I found a species of micrococcus, of unusually small size, in the blood of all persons having dengue whom I examined, which has unique biological characteristics that distinguish this from all other species of pathogenic micrococci, and make it highly probable, at least, that this microbe is causative of dengue. The unique biological habit of this micro-organism is displayed by it in the group forms that occur when it is grown in artificial culture media. These are as follows: When a culture preparation of this micrococcus is suitably stained and examined with a high power (say a $\frac{1}{12}$th homogeneous immersion lens), the picture that is presented to the eye will be made up of (1) circular groupings of cocci around a larger coccus (arthrospore) that is located in the centre of the group; (2) surrounding and imbedding the cocci will be seen a gelatinous substance—microprotein—of definite form and shape; (3) these squares of microprotein in which the cocci are imbedded join similar squares, side to side, and thus form clear and distinct filaments. The separate segments of the filament, and the micrococci grouped around a larger, centrally located coccus in each segment, can all be distinctly seen in stained preparations when examined with high-power objectives.

"Not all the filaments that can usually be seen in the same microscopic picture are perfect in form like these described. Others will be seen that are undergoing a process of disintegration, the end of which is to liberate the cocci they contain, and filaments in all stages of disintegration, from the beginning of the process to its ending and the complete liberation of the cocci, will be observed. At the beginning of disintegration the filaments appear swollen, lose their distinct outline and the markings that differentiate their parts. Then the filaments fall away, enlarge, and assume an imperfectly circular form, and finally coalesce and spread out, so that the picture they present (in stained preparations) is that of an irregular mosaic. The circular grouping of the cocci is still retained, while the microprotein which formed the principal mass of the segments retains sufficient of its outlines of these, at their points of coalescence, to produce the mosaic. Finally, as disintegration continues, all order in the grouping of the cocci disappears, and these bodies are seen scattered irregularly over the microscopic field. But it will now be observed for the first time that each coccus is surrounded by a capsule—a covering of microprotein which it brought with it from that of which the segments were composed. All the free micrococci that were seen, whether obtained directly from the blood or from artificial cultures, were encapsulated. No filaments were found in the blood that was obtained direct from the veins, and I cannot be sure they were in the blood cultures made of this micrococcus. I found many bodies having the outlines of filaments, but as I found no differentiating stain that the coccus would hold when it was washed out of the blood cells by the decolorizing washes, I cannot be sure that the bodies seen in the blood cultures were the filament-group form of this coccus obtained from other artificial cultures.

"Blood as a culture medium for this micrococcus was obtained by aspirating it directly from a vein of a dengue patient into sterilized tubes and bulbs. These were then placed in a culture oven at 100° F. and examined microscopically at different periods. All contained large numbers of the micro-organisms."

As dengue is a mild disease, it will be comparatively easy to confirm these observations of McLaughlin by inoculations upon the human subject. The question will doubtless be determined upon the advent of another epidemic.

COMMUNICABILITY.—The query as to the communicability of this disease has been so far unsettled. Its rapid and widespread diffusion seems to preclude its exclusive extension by contact of individuals. On the contrary, positive facts in evidence of its conveyance along routes of travel and from one person to another point to its being communicable. The evidence goes to show that the micro-organism which produces the disease may escape from the body of a person sick with dengue and infect another individual. Dr. Dickson states that immunity is conferred by previous attacks. He observed in Charleston that in 1850 only those escaped the disease who had suffered from it in 1828. Upon this point, however, there is no unanimity of opinion. Poggio expresses astonishment that one attack should protect so little from another. Thomas considers that once having had the disease a person is more liable to suffer from it than before, at least during an epidemic. The same author cites instances of patients who had dengue in Savannah in 1880 whom he had treated for the same disease previously.

The truth appears to be that immunity from previous attacks is much less often conferred than in most other infectious diseases.

PATHOLOGICAL ANATOMY.—Dengue being, in the vast majority of cases, a non-fatal disease, no structural changes have been noted as characteristic. In the epidemic in Galveston of 1885 my colleague, Dr. Paine, observed a localization of inflammation upon the serous membranes, especially the pleura and peritoneum, but these are to be regarded as complications rather than as usual anatomical changes.

SYMPTOMS AND CLINICAL HISTORY.—The period of incubation varies from two to five days. The onset is usually sudden. The initial symptoms are rigors or chilly sensations, headache more or less intense, pains in the muscles of the limbs and back or apparently deeper seated in the bones and joints. Coincidently there is a rise of temperature, which varies from 101° to 106° F. Anorexia is usually complete; nausea and vomiting are common; the tongue is moist and acquires a yellowish coat. The pulse and respiration are quickened in proportion to the extent of the fever, the former ranging from 95 to 120 per minute. In children convulsions may occur at the outset, and with a high temperature they are frequently delirious. The face is turgid, the eyes red and watery. The urine is rather scanty and high colored, but is rarely albuminous. Lassitude, weakness, and restlessness are usually present and proportionate to the severity of the attack. The joints are not only painful and stiffened, but in many instances swollen. These symptoms, after persisting several days, are followed in a considerable number of cases by an eruption which varies very much in appearance. Dickson describes the exanthem as appearing usually on the fifth or sixth day, and consisting of minute papulæ, somewhat elevated, of a florid red color, distributed in irregular patches. It is noticed first in the face, then on the trunk and thighs, gradually spreading to the extremities. When fully developed it is attended with some itching and burning, and generally disappears in two or three days with some desquamation. The eruption sometimes resembles urticaria or measles; ordinarily it is scarlatinous in form, but is less diffused than that of either rubeola or scarlet fever.

The exanthem, according to the writer's experience, is absent in many cases. In all probability it varies in frequency in different epidemics. During the progress of these symptoms the fever continues, the temperature rising on the second or third day to 102°, 103°, or even 105° F. It then declines and returns to normal on the fifth day. According to the observations of D'Aquin of New Orleans, "the temperature curves of dengue showed a continuous and steady rise until the highest point was reached on the first, second, or third day of the attack. Then comes a short stadium of a few hours, and then a remission, even to be followed by another rise of temperature, which, however, never reaches the maximum point of the first." The eruption generally appears with the second access of fever, and simultaneously there is inflammatory enlargement of the suboccipital, cervical, axillary, and inguinal lymphatic glands.

A disposition to hemorrhages from the mucous membranes has been noted in a considerable proportion of cases. Bleeding may take place from the nose, gums, stomach, intestines, and uterus. Menorrhagia, metrorrhagia, abortions, and miscarriages are likely to occur.

Convalescence is usually slow, and is characterized by an amount of prostration and weakness apparently out of proportion to the severity and gravity of the disease. The stomach is left in a weak and irritable condition; there are anorexia, nausea, and vomiting. Not infrequently one or two weeks elapse before a restoration to the normal vigor of mind and body is established. A better idea of the symptomatology of the disease will be obtained by a brief analysis of the more important clinical events.

The Muscular and Arthritic Pains.—Every author who has ever described dengue has called attention to the severity of these symptoms; especially is this the case if he himself has been the victim. The various names which have been given to the disease are significant as to the prominence of the rheumatoid manifestations. It is hardly necessary to remark that such events should be differentiated from true rheumatism. We have in dengue an exaggeration of what is observed in many other of the infectious diseases; that is, a predilection upon the part of the specific pathogenic agent to affect the muscular structures. There are many of the milder cases where the pain is located in the muscles, chiefly of the neck and limbs, the joints not being especially involved.

Course of the Fever.—The statement that there are two paroxysms of fever separated by an interval of complete apyrexia requires modification. It was founded, doubtless, upon the accounts of the earlier writers before careful thermometric observations had been made, the period of decided remission being taken for complete intermission. Thus Eugene Foster states that out of 500 cases seen by him in the epidemic at Augusta, Georgia, in 1880, there was but one paroxysm, lasting from four to seven days. Confirming the statement of Dr. D'Aquin, already quoted, that there was a continuous and steady rise of temperature until the highest point was reached, most frequently on the second day, then a short stadium of a few hours, then a remission, soon to be followed by another access of fever, which, however, never, reached the first maximum of heat, Dr. John Wortabet[1] in his description of the epidemic of 1883 in Syria says that the fever was continuous from three to five days, ranging from 99.5° to 104.5° F., being higher in the forenoon than in the afternoon, and that the paroxysm occurring on the sixth day was very rarely observed in the Syrian epidemic. The observations of D'Aquin have since been confirmed by Vauvray, who studied the disease in Egypt, also by Dr. Brun, who observed the epidemic which prevailed in 1888–89 in Beyrout, Syria. There are, doubtless, however, some cases, as described by Martialis of India, Thomas of Savannah, and Holliday, where there is a distinct interruption of the fever, followed by a milder secondary thermic paroxysm.

The Eruption.—During the first febrile paroxysm the *initial rash* is observed. In India this rash has been noted by Martialis and Charles as present in from one-half to two-thirds of the cases. It is usually transitory, lasting only during the first febrile period, and varies in appearance from a slight blush to a well marked erythema. The terminal rash is more constantly present than the primary one. It has no uniform appearance, and may be erythematous, miliarial, urticarial, or herpetic, and is indicative, should there be no relapses, of the decline of the disease. Upon its first manifestation there is often a slight rise of temperature; sometimes there are successive crops, and desquamation is coincident with convalescence. The frequency with which any eruption at all occurs varies in different epidemics. Unquestionably there are many cases where it is entirely absent.

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[1] *Transactions Ninth International Medical Congress*, vol. iv. p. 467.

Glandular Enlargements.—Since the time of Dickson nearly all writers on dengue have described, in connection with the eruption and appearing about the same time, inflammation of the lymphatics of the neck, axilla, groins, and elsewhere. In a brief report made by the writer upon the epidemic of 1885 in Galveston reference was made to the fact that no such glandular involvement was found in the cases then observed, but the testimony of medical friends both here and in other portions of Texas is convincing of the fact that this epidemic did not differ from those which preceded it as regards the occurrence of this symptom; and, while it may not have been noticed in the practice of several physicians, the observation of a large number of cases would show a certain proportion in which it was found.

Hemorrhages.—A disposition to bleed from various mucous membranes has been observed by a number of practitioners. My colleague, Dr. Paine,[1] in speaking of the Texas epidemic in 1885, refers to "serious hemorrhages from the colon, stomach, vagina, and uterus," and states "that the two latter organs seemed to bear the brunt of this congestive action, as manifested by the frequent sanguineous exudations from these parts. It often happened that women menstruated out of their regular term, sometimes profusely, and suffered from menorrhagia when seized at a normal epoch. Old women long past the menopause were known to lose blood from their genitalia. Miscarriages at every stage of pregnancy occurred." Foster[2] mentions hemorrhages from the nose, gums, lungs, uterus, and bowels, one instance of the latter finally proving fatal. He also mentions two cases of black vomit similar to that seen in yellow fever. As to hæmatemesis and intestinal fluxes, while there is no reason that bleeding should not occur from the stomach and bowels in a disease showing such decided hemorrhagic tendencies, the diagnosis of dengue should receive careful consideration under such circumstances. Reference to this point will be made subsequently.

Relapses.—The frequency of relapses is generally admitted as being one of the distinctive features of the clinical career of dengue. Baret and Mahé estimate the frequency of relapses at Réunion in 1869 as 15 per cent. By a relapse should be understood a recurrence of an attack after complete recovery. Relapses should not be confounded with exacerbations, which have been mentioned as occurring frequently after the remission.

Varieties.—A consideration of the symptomatology of dengue would be incomplete without a description of the varied forms which the disease assumes in the same and in different epidemics. It is on account of such differences that one writer will give prominence to one set of symptoms, and another, describing it as he observes it, will emphasize certain other phases. So far as a variety of forms is concerned, dengue does not depart in this respect from the rule observed by other infectious diseases. It is sufficiently descriptive to divide dengue into two classes: First, that mild form which runs a shorter course, two to three days, and in which such manifestations as high fever, arthritis, hemorrhages, glandular enlargements, etc. are absent; and second, the more intense form, which will in the main conform to the description herein given. As to the

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[1] *Transactions Ninth International Medical Congress*, vol. iv. pp. 470, 471.

[2] *Reference Handbook of the Medical Sciences*, vol. ii. p. 397.

denguis maligna mentioned by Charles of Calcutta, I think it will be conceded that the term "malignant" as applied to dengue is a misnomer, since the disease is a remarkable one in respect to its mildness. The writer distinctly remembers his first impressions of dengue obtained from professional friends in the epidemic of 1873, that "it was a good epidemic—good for the doctor, making many people so sick that these were compelled to send for him, and at the same time causing no one to die." So universal is the benignancy of this fever that when mortality occurs there is strong ground to suspect the accuracy of the diagnosis. But this portion of the subject will receive further notice.

COMPLICATIONS AND SEQUELÆ.—Considering the amount of suffering and discomfort incident to dengue fever, the comparative absence of serious complications and sequelæ is somewhat unique, aside from those symptoms which have been mentioned, such as occasional convulsions in children, a disposition to abortion, uterine and other hemorrhages, rarely a pleurisy or peritonitis. The explanation of the fact lies in the non-affinity of the infection for such vital organs as the brain, lungs, heart, or kidneys.

Convalescence is frequently characterized by anorexia, an irritable stomach, and an extent of muscular weakness and nervous depression apparently out of proportion to the duration and gravity of the disease.

DIAGNOSIS.—The ensemble of symptoms as above outlined ordinarily renders the recognition of dengue an easy matter: especially is this the case during the progress of an epidemic; but sporadic cases or epidemics occurring coincidently with yellow fever, influenza, typhoid and malarial fevers are not so easily differentiated. Any one having practical experience during the combined prevalence of these fevers can readily understand that they may be frequently confounded even by expert diagnosticians.

Differential Diagnosis between Dengue and Yellow Fever.—The idea that these two diseases are identical, or at least that dengue was a modified yellow fever, was never tenable, but was nevertheless held by a number of reputable physicians who had studied the maladies at the bedside. The facts giving currency to this view are briefly as follows: Dengue often prevails concurrently with, precedes, or follows an epidemic of yellow fever. The two diseases have similar (though not identical) geographical distribution, follow like isothermal lines, and are affected by similar climatic and seasonal influences. The clinical events of mild cases of yellow fever may so closely resemble those of dengue as to justify Porcher[1] in this statement: "It is a significant fact that we have never been able to distinguish accurately between the two—to say of every case and at every stage of these two diseases, 'This is yellow fever, this only break-bone;' yet the well marked examples of undeniable yellow fever were as different in every material aspect from lighter forms of break-bone coexisting with it as black is from white." The following table, arranged from the presentation of the facts by Foster, will serve to accentuate the distinction between the two diseases, and at the same time, show the points wherein they resemble each other: in spite of their similiarity, the fact that dengue and yellow fever are entirely different diseases cannot be too strongly emphasized:

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[1] *Transactions American Public Health Association*, art. xxxviii.

Yellow Fever.	*Dengue.*
Arrested by severe frost.	Arrested also by frost.
One febrile paroxysm characterized by a steady rise and lasting about three days.	Usually one paroxysm, but sometimes two; a steady rise of temperature until the acme is reached; a short stadium, followed by a remission, then a second rise. Duration, five to eight days.
Stomach irritable, vomiting frequent.	Vomiting not so frequent.
Tongue, white centre, red edges, pointed.	Tongue white, yellowish, rarely red edges.
Pulse slows while temperature rises.	Pulse increases in rapidity with rise of temperature.
Eruption rarely or never present.	Eruption present in the majority of cases.
Jaundice usually present.	Jaundice extremely rare.
Urine albuminous and often suppressed.	Urine free from albumin and never suppressed.
No involvement of lymphatic glands.	Lymphatic glands involved in some cases.
Hemorrhagic tendency frequent, alarming, and terminal.	Tendency to hemorrhage comparatively rare, and, as a rule, insignificant.
Often fatal.	Proverbially non-fatal.
Not protective against dengue.	Not protective against yellow fever.
Usually confers immunity against subsequent attacks.	Not generally protective against a second attack.

To illustrate the practical nature of this subject and of the close resemblance between dengue and yellow fever, it is worth mentioning that upon the report of an outbreak of dengue at Key West in August, 1893–94, it was thought by Dr. Swearingen, the Health Officer of Texas, to be sufficient reason to temporarily quarantine against that port; which action led to some controversy with the health officials of Florida. Dr. Swearingen[1] based his procedure upon the grounds that "dengue, while not generally regarded as a quarantinable disease, has been so often associated with yellow fever, by making its appearance sometimes just prior to that disease, and closely resembling it in certain manifestations, and by its appearance in Key West concurrently with yellow fever in Havana, with which city Key West is in near proximity and close relations, that in the interests of public health in Texas it was thought best to take no risks until sufficient time had elapsed to demonstrate the safety of resuming intercourse." In all cases like this the public should have the benefit of the doubt, and the action of Dr. Swearingen was perfectly satisfactory, justifiable, and wise.

Differential Diagnosis between Dengue and Influenza.—It would be interesting to draw a similar line of comparison between dengue and epidemic influenza. The points of resemblance are—the rapid and widespread diffusion, affecting all classes, all ages, and all conditions with indiscriminate violence; the frequency of relapses and liability to repeated attacks; the want of harmony between the apparent severity and small mortality of uncomplicated cases; the sudden onset, the character and intensity of the pains, and the disproportionate mental and physical depression during the period of convalescence. The points of distinction are—the differences in geographical distribution, climatic and seasonal influences; the absence of eruption in influenza except herpes; the absence of remission or intermission of the fever in influenza; the usual involvement of the air-passages in the latter and its non-occurrence in dengue; the greater frequency and severity of complications and sequelæ in influenza. It is easy to see, however, that the two diseases might readily be confounded.

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[1] *Texas Sanitarian*, Austin, Dec. 24, 1894, p. 65.

Typhoid Fever and Dengue.—At first thought one would hardly suppose that dengue and typhoid fever would ever be confused, the two disorders being so dissimilar; yet that such confusion may occur when both are epidemic will readily appear. At the close of the epidemic of dengue in 1885 in Galveston numerous cases were reported by several physicians, denominated as typho-dengue. The clinical events narrated were fever of long duration (three to six weeks), intestinal hemorrhages, suppurative inflammation of the parotid glands, and in quite a number a fatal ending. The writer contended in a discussion of these cases before the Galveston County Medical Society that the term typho-dengue was a misnomer; that the disease described was genuine typhoid fever; and that it was proven to be such chiefly by its duration, the gravity of the symptoms, and its mortality. The confusion arose from the previous rarity of enteric fever, and the occurrence of a mild epidemic at the close of a more extensive one of dengue.

Malaria and Dengue.—Dengue may also be confounded with malarial fever: especially is this so in regard to sporadic cases of the former or at the commencement of an epidemic of dengue when the latter is prevailing. The differences in the febrile movement, the absence of eruptions in malaria, the rapid supervention of anæmia, and the presence in the blood of the hæmatozoön, suffice to establish the distinction, though the writer could relate cases where it was by no means easy to make a differential diagnosis.

PROGNOSIS.—The prognosis is almost invariably favorable. Attention has been called to the fact that every author who has written upon the subject, perhaps without exception, has described dengue as a mild disease and without mortality except as the result of an intercurrent or rather accidental complication, such as convulsions in weakly children and septicæmia from a badly treated abortion. So when we hear of deaths from dengue as a result of intestinal hemorrhages or from black vomit, or any other causes, we should view the diagnosis with suspicion. The fact alone that the so-called dengue is attended by mortality is sufficient cause to call in question the diagnosis.

TREATMENT.—It is useless to discuss the old antiphlogistic plan of treatment—general bleeding, active emeto-cathartics, etc.—as it has very properly been discarded. The attempts to prevent attacks during an epidemic by the use of quinine have been proven to be entirely ineffectual. Quarantine measures, except when there is a suspicion of yellow fever, are not likely to be enforced at present, but the time may come when even this disease, though universally acknowledged to be non-fatal, will be controlled in its march to a great extent by governmental authority. We do not as yet know to what extent this can be accomplished, but, judging by its method of dispersion, there is reason to believe in the probability of such restriction.

Medicinal Treatment.—The disease being self-limited, the indications are to relieve the symptoms. If the stomach is full at the time of attack, a mild emetic would not be out of place. Apomorphia, one tenth of a grain hypodermically, will act with certainty and rapidity, or the older emetics, ipecacuanha, mustard, salt, and warm water, which are handy, may be used. The bowels ordinarily require attention, though excessive purgation is not desirable. Moderate doses of calomel, five to six grains in a single dose, or the same quantity divided into several smaller doses, has the effect, when the bowels are moved, to relieve the nausea and headache by its revulsive and evacuant action, as well as to favorably affect the alimentary canal for assimilation and absorption. Many practitioners prefer to prescribe a more rapidly acting purgative, as some of the salines, emulsions of castor oil, etc. To relieve the intense headache a hot mustard foot-bath at the outset is of decided service. The different coal-tar antipyretics are indicated for the relief of the rheumatoid pains, as well as to reduce excessive fever, and can be employed according to individual preferences. While quinine cannot be depended upon as a prophylactic, it aids in controlling the pyrexia and pains, besides having a tonic effect. The salicylates are also useful analgesics. A very good combination at the outset would be the following for adults:

℞. Calomel,	6 grains;
Phenacetin,	½ drachm;
Quinine bisulphate,	15 grains.

Mix and divide into ix capsules.
Sig. Take three capsules every three hours.

After the above, phenacetin with quinine, ten grains of the former to five grains of the latter, may be continued every four to six hours according to the temperature and severity of the pains. When the pain is unusually acute opiates may be required. Morphia and atropia given hypodermically afford the quickest relief. Salicylic acid or salicylate of sodium is objectionable on account of the disagreeable head symptoms and nausea frequently produced by either medicament. Salophen, however, is free from these objections, and is a useful addition to the phenacetin and quinine; it may be given in doses of ten or fifteen grains according to the effects produced.

Active hydrotherapy—that is, the use of cold baths—is ordinarily not required. Warm baths, however, having the water at a comfortable temperature—say from 90° to 95° F.—allay nervous excitement and generally add to the well-being of the patient. Cold applications to the head and sponging the body with tepid evaporating lotions, as of alcohol and water, assist in accomplishing the same results. Irritability of the stomach generally subsides when the bowels have been freely moved. If this symptom is obstinate, iced champagne, Vichy and Apollinaris waters, subnitrate of bismuth, dilute hydrocyanic acid, with sinapisms to the epigastrium, are remedies and measures which are indicated. Turpentine stupes and anodyne embrocations assist in relieving the rachialgia. The diet ordinarily should consist of milk, meat broths, and gruels. Lemonade and orangeade are grateful to the taste. To relieve the depression of convalescence the moderate and careful use of alcoholic stimulants, with such reconstructives as the phosphates of iron, quinine, and strychnine, essence of calisaya, Ducros' elixir, etc., are often required and subserve a useful purpose.

ENTERIC OR TYPHOID FEVER.

BY J. C. WILSON, M. D.

DEFINITION.—An acute, infectious disease, characterized clinically by a febrile movement varying in duration from twenty-one to twenty-eight days, by gastro-intestinal catarrh, marked prostration, rapid wasting, marked nervous symptoms, and a scanty eruption of isolated, slightly elevated, rose-colored spots, which disappear upon pressure and are developed in successive crops; anatomically by constant lesions of the lymph-follicles of the intestines, enlargement of the mesenteric glands and of the spleen, and parenchymatous degeneration of the viscera. Eberth's bacillus is present in the lesions.

SYNONYMS.—To enteric fever many names have been applied. It is called by the Germans "typhus abdominalis" to differentiate it from true typhus—"typhus exanthematicus." Louis, in 1829, gave to the disease the name of "typhoid fever" (*fièvre typhoide*), a designation that has since passed into almost universal use. To the name "typhoid," however, there are the same objections that apply to the "typhus abdominalis" of the Germans, as both terms would imply a relation to typhus fever which exists neither clinically nor anatomically. Although no longer in use, the term "slow nervous fever" of Huxham's day is finely descriptive. Other names still occasionally loosely used are "gastric fever," "intestinal fever," "ileo-typhus," and "infantile remittent fever." The last was at one time employed to designate the fever as it occurs in early childhood. The disease at this period of life is characterized by marked remissions in its temperature range, and was for a long time regarded as a distinct affection not in any way related to enteric fever, from which infants and young children were supposed to enjoy a high degree of immunity. Later investigations, however, proved the erroneous character of these views and established the identity of the so-called infantile remittent fever with enteric fever.

"Enteric fever" seems the most appropriate name for the affection. It indicates at once the site of the constant and most important of the gross lesions, and by the use of the term "fever" coupled with the adjective, the infectious character of the process. For these reasons, and because it is not open to the objections that may be urged against "typhus abdominalis" and "typhoid," it is now extensively employed among English-speaking physicians, and especially in army and navy medical circles and in government reports.

ETIOLOGY.—Enteric fever is due to the implantation in a susceptible organism of a specific infecting principle—the bacillus of Eberth.

Predisposing Influences.—These constitute, first, all conditions which favor the development and accumulation of the infecting principle, and, second, those conditions which increase the susceptibility of the individual to the cause of this particular fever and the liability of his exposure to it.

The *geographical distribution* of enteric fever is wide. This disease prevails in all countries and in every climate. It is, however, especially prevalent in temperate climates. It is the great fever of the present historical epoch, just as the plague was in Europe the great fever of the Middle Ages and typhus the great fever of the seventeenth and eighteenth centuries. Enteric fever is endemic in the British Islands, in Continental Europe, and in North America. Hirsch has reached the conclusion that the general prevalence of this disease in Europe and America dates no farther back than the second and third decades of the present century; that is, from the period which typhus (*der Petechial Typhus*) ceased to prevail generally and in many localities disappeared altogether. In America enteric fever prevails from Hudson Bay to the Gulf of Mexico. In newly settled districts, where the land is being gradually brought under cultivation, the malarial fevers are common; after a time, as populations increase, the malarial diseases and enteric fever prevail side by side; finally, when the land has been generally taken up, drained, and tilled, and villages and cities abound, true agues and remittents largely disappear, while enteric fever becomes the usual endemic fever, common in proportion to the neglect of the sanitary measures by which alone it can be kept in check.

Climate, not directly, but as determining the mode of life in communities, has much influence upon the extent of the prevalence of enteric fever.

The *season* of the year is a predisposing influence of great importance. About 50 per cent. of the cases occur during the months of August, September, and October. The number of cases decreases during November and December, is lowest from February to May, again increasing in June. This fever is so much more common in the latter part of the year that it is known in some districts of the United States as "autumnal" or "fall fever."

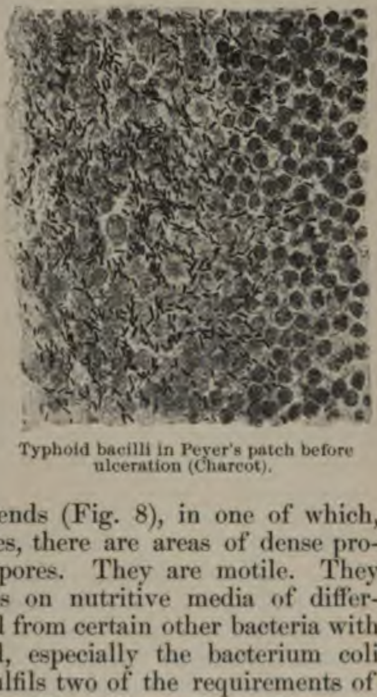
The *weather,* as regards dryness and moisture, exerts a decided influence upon the prevalence of enteric fever. Its prevalence is greater during hot and dry seasons; less during cool and wet summers. Outbreaks of enteric fever in localities supplied by surface water or shallow wells have frequently followed abundant rains.

Age is of great importance among the predisposing causes. Enteric fever is especially a disease of adolescence and early adult life. The period of greatest susceptibility is between the ages of fifteen and thirty, the liability diminishing progressively both above and below these limits. In 1864, Murchison demonstrated at the Pathological Society of London the intestines of an infant six months old who had been attacked at the same time with her mother. Cases in the first year of life are, however, exceedingly rare, but from the termination of this period the liability gradually increases through infancy and childhood. The explanation of the fact that the proportion of the cases occurring in infancy is smaller than that of childhood and adolescence is found in the greater exposure to the cause of the disease in the later periods. Enteric fever is not common in advanced life. I have, however, seen cases in the fifty-eighth and sixty-ninth year. This immunity is to be accounted for by the fact that a large proportion of individuals surviving to the later periods of life have previously suffered from the disease.

Sex exerts no predisposing influence. The disparity shown by statistics is due to the fact that a greater number of males than females suffering from acute disease are admitted to hospitals. Certain statistical series would appear to show that the disease is more frequent in boys than in girls. These statistics fail to embody the fact that beyond the age of infancy girls are much less exposed to the infection than boys. The latter, in their outdoor sports—bathing, swimming, and the like—incur especial risk in drinking water directly defiled by sewage.

The *mode of life* is without influence. Enteric fever is as apt to occur in the houses of the affluent as in the most crowded and destitute localities. The prevalence of enteric fever in the great centres of population diminishes in proportion as protection of the water supply advances and sewer systems are improved. In rural districts where sanitary regulations are ignored the disease appears to be upon the increase. I have knowledge of several suburban localities in which enteric fever, for many years prevalent, has wholly disappeared within a short time after the introduction of artesian water and the abandonment of shallow wells.

FIG. 8.



Typhoid bacilli in Peyer's patch before ulceration (Charcot).

The Exciting Cause.—The micro-organism described by Eberth, Koch, Gaffky, and others, and known as the *bacillus typhosus* or *bacillus typhi abdominalis*, is at the present time generally accepted as the cause of enteric fever. This organism is constantly present in the specific lesions of the disease. The bacilli are about one third the diameter of a red blood-corpuscle in length and about three times as long as broad—2.5 by 0.8 μ. They are blunt and rounded at the ends (Fig. 8), in one of which, sometimes in both, especially in cultures, there are areas of dense protoplasm that have been regarded as spores. They are motile. They can be readily grown in pure cultures on nutritive media of different kinds, and can be now differentiated from certain other bacteria with which they were formerly confounded, especially the bacterium coli commune. This bacillus completely fulfils two of the requirements of the law formulated by Koch in regard to the evidence that a disease is caused by a given micro-organism: it is present in every case of the disease and in such distribution as will explain the specific lesions, and it can be isolated in pure culture. The third requirement of the chain of evidence, that the disease must be reproduced by inoculation of the isolated organism, remains unfulfilled. The results of inoculation experiments have in most instances been due to the toxic rather than the infective properties of the inoculated substance. It has therefore been concluded that the lower animals are not susceptible to enteric fever. The fact that hyperplastic and ulcerative lesions of the lymph structures of the intestines have followed such inoculations is not conclusive, since it has been shown that similar lesions may be caused by the bacterium coli commune and other micro-organisms.

Abbott in a number of experiments upon rabbits obtained a single positive result. In this case there was an ulcer in the ileum identical with those found in the intestines in the human subject, and typhoid bacilli were demonstrated in characteristic clumps in sections of the spleen and were obtained from that organ by culture methods.

The difficulties regarding the subject are not insurmountable. Recent researches have shown that definite toxic and immunizing substances are produced by this bacillus. These results tend to support the view already almost universally accepted, that the organism in question is the specific cause of enteric fever.

The bacilli have been found in the blood, especially in that drawn from the spleen and the rose-colored spots. They tend, however, to colonize in clumps in the lymph-tissues of the intestines, in the mesenteric glands, in the spleen, in the marrow of the bones, and in the liver. They have been found in the bile, in the urine, more abundantly when it is albuminous, and in the sweat. They have been isolated from endocardial vegetations and from serous and purulent exudates in different parts of the body. They cannot be discovered in the stools until the tenth, sometimes not until as late as the sixteenth, day. In fatal cases cultures of the intestinal contents have frequently given negative results.

The most active existence of this organism is parasitic. It is, however, a facultative saprophyte, and is capable of a prolonged existence under favorable circumstances both within the body of the patient who has suffered from enteric fever and outside of the human organism. Outside the body it retains its vitality for a variable period of time. The extreme duration of this period is not known. In ordinary water it is measured by weeks. Hochstetter found typhoid bacilli capable of growth after they had been for twelve days in a siphon of seltzer water. They survive longer in closed cisterns and reservoirs than when exposed to light, and Janowsky has shown that cultures cease to develop after some hours of exposure to sunlight. That they retain their vitality in running water has been shown by the history of many epidemics. Prudden found them capable of culture after having been frozen in ice for several months and after repeated freezing and thawing. Prudden and Ernst found them in the water-filters of houses in which cases of enteric fever had developed. Whether or not they increase in ordinary water remains unsettled. It is generally believed that some increase does take place. They grow luxuriantly in milk without causing coagulation or changing its appearance in any respect. They retain their vitality for months in fecal matter, and many local outbreaks have been traced to the disturbance of privy-vaults into which the stools of enteric-fever patients have been previously emptied. Uffelmann has shown that typhoid bacilli have a remarkable vitality and tenacity in dried fecal matter. They not only continue to live, but also grow and multiply, upon the surface of the soil, and where the ground is frequently moistened they penetrate to a considerable depth, retaining their vitality. There is, however, no proof that typhoid bacilli are capable of an indefinite existence outside the body, much less of an indefinitely prolonged independent and vigorous non-parasitic growth. On the contrary, there is reason to believe that sunlight, dispersion, the action of putrefactive bacteria (Karlinski), and unsuitable or insufficient pabulum would ultimately lead to their extinction were it not for constant renewal by the infection of fresh cases.

The germs find access to the body by way of various ingesta. If, as exceptionally appears to have been the case, they are inhaled with particles of dust floating in the air, it is probable that they become entangled in the secretions of the mouth or pharynx and are swallowed. The common vehicle is drinking water which has been defiled by sewage. The endemic prevalence of the disease in cities and many local epidemics are to be attributed to this cause. Even water that has been recently boiled may take up germs from a contaminated filter or from contaminated ice.

Many local epidemics have originated in the pollution of the water supply by a single patient. Among these none is more important than the well known epidemic at Plymouth, Pa., in 1865. A portion of the water supply of the town was derived from a reservoir filled from a mountain stream some distance above. A case of enteric fever occupied a house upon the banks of this stream during January, February, and March. The copious dejections of this patient were thrown upon the ground, which was at that time frozen and covered with snow. Toward the end of March a thaw, accompanied by a rainfall, took place. About the 10th of April an epidemic of enteric fever developed in the town, chiefly among the inhabitants whose water supply came from the reservoir. In a population of 8000 people 1200 cases occurred.

The following personal observation illustrates a very common mode of the propagation of enteric fever: A physician developed the disease under the following circumstances: His house stood upon a small lot in a village at the time and for a long time previously free from enteric fever. Early in September the patient's brother came to his house ill with enteric fever. The dejections from this case, treated with a small amount of a so-called commercial disinfectant, were thrown into the privy, an ordinary open vault such as is common in country places. The well from which the drinking water for the household was obtained was about twenty-five paces distant. Toward the close of September the physician fell ill with enteric fever, and within a few days three other cases occurred in his household.

Infection is less common by the way of milk, in which the germs grow luxuriantly without altering its physical characteristics. A number of epidemics have been traced to this cause. The infection in these cases cannot be traced to disease in the cow, but to an admixture of defiled water with the milk, either intentionally or as the result of its use in cleansing milk-cans. The transmission of the infecting principle by milk was definitely established by the investigations of Ballard during a local epidemic at Islington in 1871. The outbreak was shown to be due to the employment of water defiled by direct communication with drains for the purpose of washing the milk-cans.

Circumscribed epidemics have occurred in which the most careful efforts to trace the source of the disease have been without positive result. In an outbreak a few years ago in a military academy in the neighborhood of Philadelphia this was the case. Among 132 students 14 cases developed in rapid succession. The infection was virulent, 5 of the 14 cases terminating fatally. One of the patients came under my observation, and subsequently recovered in the German Hospital of Philadelphia. Painstaking investigations conducted by competent observers failed to reveal the source of infection. A theory that the first case was due to infected milk obtained at a shop in a neighboring city could not be established.

The possibility that typhoid bacilli may be present on the surface of raw vegetables or other articles of food that have been washed with water containing them is not to be overlooked. Articles of food may be contaminated by the soiled fingers of the patient himself or of his attendants.

The bacilli may be transported from the fecal discharges of a patient to articles of food by means of house-flies. Oysters "plumped" or freshened for market by exposure for a short time in the fresh water of streams defiled by the sewage of towns or cities may become infected. Conn has reported an epidemic at Middletown which he attributes to the eating of uncooked oysters infected in this way. Foote found in river oysters a larger number of micro-organisms than in those from the sea. He showed that the bacillus typhosus preserves its vitality in the brackish water in which oysters are laid down, and for a longer time in the oyster itself.

It was at one time thought that the infecting principle of enteric fever was not immediately capable of giving rise to the disease, but that its pathogenic properties were acquired in the course of a short time in consequence of changes after leaving the body. In accordance with this view enteric fever was regarded as a contagious miasmatic disease. The theory of Pettenkofer that the poison is not eliminated in a condition capable of immediately giving rise to the disease, but that it acquires its pathogenic properties in consequence of changes in the soil, and that these changes are favored by the action of the ground water, is of a similar nature. These theories are no longer tenable.

The doctrine of Murchison and his followers that the specific cause of this disease may be generated *de novo* in decomposing sewage in which the discharges of enteric fever patients are not present is likewise untenable. It is true that filth, defective sewers, cesspools, and soils contaminated with fecal matter favor the accumulation of typhoid germs, and in some cases supply media for their growth, but these conditions cannot, in the absence of the specific infecting principle, give rise to enteric fever. There is no proof whatever that this disease in the absence of the germ referred to can be generated by the products of decay or decomposition, by sewer exhalations, by tainted food, or by the action of other bacteria.

By far the largest proportion of the bacilli are without doubt destroyed within the body. The remainder find their way out in the stools, to a slight extent in the urine, very rarely in the vomited or expectorated matters or the perspiration. They are not eliminated by the expired air. Enteric fever cannot therefore be regarded as contagious in the ordinary meaning of the term. It is communicable by the infecting principle contained in these matters, but chiefly in the fecal discharges. This infecting principle is invariably derived either directly or indirectly from a previous case.

Sporadic cases of enteric fever occasionally occur under circumstances that baffle explanation. This has sometimes been the case among small bodies of troops in practically uninhabited districts, as in border campaigns. The suggestion that the infection under these circumstances has taken place by means of typhoid bacilli in condensed milk or other articles of food, and that the immunity of those who escape is to be ascribed to previous attacks of enteric fever, is plausible. The alternate suggestion that the infecting principle of enteric fever is a germ widely diffused in nature, and that it acquires pathogenic properties when developed in contact with decomposing fecal or other organic matter, has not met with general acceptance.

PATHOLOGICAL ANATOMY.—The typhoid bacilli, gaining access to the organism by way of the gastro-intestinal tract, enter the lymph structures of the intestines and there develop, elaborating toxic principles to which the constitutional phenomena are due. Brieger, Fränkel, and others have isolated from bouillon cultures of the bacilli a toxalbumin to which the term typho-toxin has been applied. The fact that typhoid bacilli are not found in the fecal discharges in the early course of the disease, but first appear about the time of the necrosis of the lymph elements, justifies the assumption that the bacilli do not develop, as do those of cholera, within the lumen of the gut.

The constant and characteristic gross anatomical changes of enteric fever are to be studied in the solitary and agminate glands of the intestines, especially at the lower end of the ileum, in the associated lymphatic structures of the mesentery, and in the spleen.

Anatomical Changes in the Intestines.—The anatomical changes in the intestines may be divided into four stages.

1. *The Stage of Infiltration or Hyperplasia.*—In this stage swelling of the solitary and agminate glands takes place, and is due to hyperplasia of their elements, the surrounding mucous membrane being intensely hyperæmic. The agminate glands are distinctly elevated above the surrounding surface, and after the early hyperæmia and congestion have disappeared become grayish white or opaque in appearance, with a slightly rough, irregularly mammillated surface. The solitary follicles are not invariably affected, but when affected they constitute shot-like projections from an eighth to a quarter of an inch in diameter. The hyperplasia of the lymph elements extends deeply into the submucous tissue, but at the borders it is limited, so that both the solitary and agminate lymph follicles are distinctly differentiated from the surrounding mucous membrane by abrupt margins. The whitish or opaque appearance of the glands is due to the compression of the bloodvessels: nor is the infiltration limited to the glands, but may proceed deeper, involving the submucous, the muscular, and even the serous layers of the intestine.

The infiltration attains its maximum development some time between the end of the first week and the tenth day of the disease. At this stage of the process the anatomical change may cease and resolution take place; if, however, as is commonly the case, the bloodvessels have become so choked that repair is impossible, necrosis of the lymph structures results.

In children hyperplasia of the lymph follicles is not uncommon in intestinal diseases. It occurs also in scarlet fever, measles, and diphtheria. While, therefore, hyperplasia of the lymph follicles is not peculiar to enteric fever, a marked enlargement of these structures is rarely seen in adults in any other febrile affection.

2. *The Stage of Necrosis.*—The hyperplasia of the lymph follicles advances. Resolution is no longer possible. Mechanical interference with the blood supply from the pressure of the infiltrated tissues, the growth of the bacilli, and the direct action of the concentrated toxic principles evolved at the seat of their activity are factors in bringing about rapid and more or less extensive necrosis in the affected glands. The swollen patches and discrete follicles undergo sloughing, which, on the one hand, may be superficial, involving only the epithelial and subepithelial structures, and, on the other, may extend to and involve the peritoneal coat of the intestine. Between these extremes necrosis of varying depth occurs, the muscularis commonly, but by no means invariably, limiting the process. The infiltration and necrosis are progressively more marked toward the lower end of the small intestine, and in severe cases the mucosa of the ileum for some inches above the ilio-cæcal valve is extensively gangrenous. The attached sloughs are of a grayish-white color, or they may be stained yellowish brown or green by the intestinal contents, especially the bile; sometimes, being infiltrated with blood, they are dark in color. The separation of the sloughs takes place during the latter half of the second and the course of the third week.

3. *The Stage of Ulceration.*—The sloughs are gradually detached, separation taking place first at the borders. Ulcers of varying depth and of a size and form corresponding to the necrotic tissue are thus formed. If an entire patch be involved, the resulting ulcer is elliptical, of considerable size, and situated opposite the mesentery, its long axis corresponding to the long axis of the bowel. It is more common to find irregularly circular or ovoid forms which occupy a portion only of the Peyer's patch, or two or more irregularly bordered forms of ulceration separated by bands of mucosa. Very extensive ulceration is sometimes encountered just above the ileo-cæcal valve. The edges of the ulcers are usually abrupt, the surrounding tissues being thickened and often overhanging. Their bases may be formed by the submucosa; more commonly they are formed by the muscularis, sometimes by the serosa, and in those instances in which the necrosis involves the peritoneum the wall of the gut may slough out through its entire thickness. Ulcers resulting from necrosis of the solitary follicles are usually small and round. When death has occurred late in the course of the attack irregular, serpiginous ulceration is in some instances observed.

4. *The Stage of Cicatrization.*—The swelling in the edges of the ulcers gradually diminishes, the base becomes covered with a delicate layer of granulation tissue, and the mucosa extends over the healing surface, which is ultimately invested with epithelium. The gland structure is

to some extent re-formed. The resulting scar is slightly depressed, usually pigmented, smooth and less vascular than the surrounding mucosa. It has no tendency to contract or pucker or to narrow the lumen of the gut. When cicatrization progresses in this favorable manner the time occupied by the process of healing is probably about a fortnight. Lesions are sometimes seen in which cicatrization is going on in one place while in another active ulceration is in progress. When death occurs during a relapse patches of active ulceration coexist with the nearly healed ulcers of the primary attack.

The solitary glands of the cæcum and colon are involved in a considerable proportion of the cases. The appendix may also be the seat of ulceration. Perforation of the cæcum is a rare event. The lesions of the lymph structures of the intestine do not in all instances go on to necrosis. It is probable that resolution without extensive necrosis takes place in the abortive cases and in many of the cases in childhood. This process results from fatty and granular changes in the cells which undergo destruction and are absorbed.

There is associated with these lesions catarrhal inflammation of the large and small bowel, to which must be ascribed many of the intestinal symptoms, and in particular the diarrhœa.

A limited number of cases have been reported in which the symptoms of enteric fever have occurred, but upon section the intestinal lesions have not been found, although the mesenteric glands, spleen, and kidneys have been enlarged and congested. The presence of the bacilli of Eberth in the affected organs is necessary to the diagnosis of enteric fever.

Hemorrhage from the bowels occurs in about 5 per cent. of the cases. It occurs at the time of the separation of the sloughs. The frequent occurrence of large, even fatal, hemorrhages points to the implication of arterial twigs of some size in the necrotic process. Adherent clots may be found at the source of the bleeding. Oozing of blood may occur from the swollen borders of the ulcer.

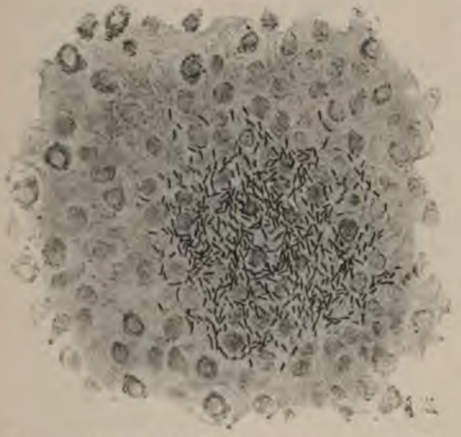
Intestinal perforation occurs with about equal frequency. The opening may be round or "punched out" or slit-like and linear. In the former case it results from the separation of a slough that has involved the wall of the gut throughout its entire thickness, including the peritoneum; in the latter from tearing of the base of an ulcer extending to the peritoneum in consequence of active peristaltic movement. Perforation occurs more commonly about the time of the separation of the sloughs, but it may take place some weeks after the defervescence. In a majority of instances perforations are single, but two or more may be present. Their usual site is within ten or twelve inches of the ileocæcal valve. Perforations of the cæcum and of the appendix are less common. The escape of intestinal contents is followed by infection of the peritoneum and general peritonitis.

THE MESENTERIC GLANDS show histological changes similar to those in the intestinal lymph structures. In the early stages they are hyperæmic and enlarged; later they become pale, and not infrequently limited necrotic areas are found, especially in the central portion of the glands. In the majority of instances the lesions in the glands of the mesentery undergo complete resolution. Occasionally they soften or undergo cheesy changes. They may ultimately be converted by the deposition of lime salts into hard, calcareous masses. In other instances softening of the mesenteric glands may result in the formation of pseudo-abscesses, the walls of which may rupture and give rise to fatal peritonitis.

Other lymphatic glands may undergo enlargement, notably those in the fissure of the liver, the retroperitoneal glands, and the bronchial glands.

The SPLEEN is enlarged in over 90 per cent. of the cases of enteric fever. Its structure shows changes analogous to those in the lymph follicles of the intestines in the earlier stages of the disease. It is soft, pulpy, and may be even diffluent. Upon section the surface is brownish red in color, and hemorrhagic infarcts are frequently found. It is liable, when greatly softened, to be accidentally ruptured by palpation, or this accident may even occur spontaneously. Rupture of the spleen occurred in five instances among two thousand autopsies at the Munich Pathological Institute.

FIG. 9.



Human spleen, tenth day of enteric fever (Charcot).

The enlargement of the spleen may be usually recognized toward the end of the first week. It reaches its maximum about the fourteenth day, when the organ will be found to be two or three times its normal size. During the fourth week or with the occurrence of defervescence involution rapidly takes place, and by the end of the fifth week the organ has returned to its normal dimensions. Persistent splenic enlargement after defervescence points to the possibility of a relapse. Enlargement of the spleen does not occur in many of the cases in advanced life: it may also be absent when the capsule has become thickened as the result of previous inflammation, with the formation of firm adhesions to adjacent structures.

The LIVER early in the course of the disease is hyperæmic and slightly enlarged. Later it is somewhat pale and less consistent than normal. The minute changes are those of parenchymatous degeneration; the liver cells are granular, crowded with fat, and the nuclei indistinct, often entirely absent. Very rarely the liver presents an appearance resembling that of acute yellow atrophy.

Certain peculiar changes occurring in the liver have been described, notably by Wagner, who applied to them the term "lymphoid nodules," and Handford called attention to the existence, late in the disease, of small necrotic areas.

Investigations recently conducted by Walter Reed in the pathological laboratory of the Johns Hopkins University[1] show that the lymphomata of Wagner are in reality areas of necrosis. As to whether they are due to the direct action of the bacillus of Eberth or are caused by the action of toxalbumins has not, as yet, been definitely determined. The latter explanation is regarded by Reed as the more probable, in view of the fact that Welch and Flexner[1] have produced in the liver of guinea-pigs well marked necrotic areas by the injection of the toxalbumins of diphtheria.

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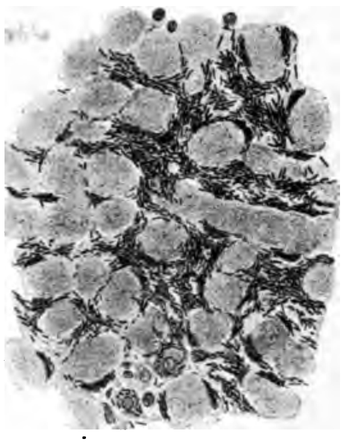
[1] *Am. Journ. Med. Sciences*, November, 1895.

Fig. 10.



Human liver, tenth day of enteric fever (Charcot).

Pylephlebitis with resulting abscess of the liver is an exceedingly rare complication. Lannois[2] recently reported a case of enteric fever in which there occurred pylephlebitis and multiple hepatic abscesses, the presence of the bacillus of Eberth being demonstrated in the pus. As a result of his studies of this case and of the literature upon the subject the conclusion is reached that the complication is a rare one. Catarrhal or diphtheritic inflammation of the gall-bladder may be encountered.

Kidneys.—Parenchymatous changes occur. They consist of cloudy swelling with granular degeneration of the cells of the convoluted tubules. Acute nephritis is an occasional complication. Disseminated areas of round cell infiltration corresponding to the so called lymphomata of Wagner in the liver and sometimes proceeding to softening have been observed. When suppuration occurs the appearance is that presented by miliary abscesses. Typhoid bacilli have been found in these minute collections of pus. Diphtheritic inflammation of the pelvis of the kidney is of rare occurrence. The bacilli have been found in the non-albuminous urine, more commonly when albumin is present and in cases of pyuria.

Catarrh of the bladder is by no means infrequent. Diphtheritic cystitis is rare. Purulent cystitis is usually due to the use of uncleanly catheters. Epididymitis is more apt to occur in cases that have required catheterization.

The Heart and Bloodvessels.—Endocarditis occasionally occurs. It is usually slight. Of two thousand post-mortem examinations at the Munich Pathological Institute[3] it was present in eleven instances. Pericarditis is also a rare lesion in enteric fever, being found, according to the same statistics, in fourteen cases.

The myocardium shares in the general wasting which accompanies the disease. The muscle of the heart is relaxed, flabby, and atrophic. When the organ is removed from the body and placed upon the post-mortem table it flattens out. Microscopically, there is found granular and fatty degeneration with small-celled infiltration; the fibres are indistinctly striated or the striation is lost and they are translucent and granular.

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[1] *Johns Hopkins Hospital Bulletin*, 1892, vol. iii. No. 20.

[2] *Revue de Médecine*, 1895, No. 11, p. 909.

[3] *Münchener medicinische Wochenschrift*, Nos. 3 and 4, 1891.

The arteries are frequently implicated in the pathological processes of enteric fever. Obliterating endarteritis occurs. It more commonly affects the vessels of the lower extremities. Endarteritis of the smaller vessels, especially of the coronary arteries, is not uncommon. Proliferating endarteritis involving the smaller vessels was found by Dewevre in 3 of his series of 48 cases. Venous thrombi occur. They are relatively common in the femoral veins; less so in the cerebral veins and sinuses.

The **voluntary muscles** frequently show granular and fatty changes. These changes occur in other infectious febrile diseases and are not peculiar to enteric fever. Rupture of bundles of muscle fibres sometimes takes place, giving rise to hemorrhage into the muscles, and, less frequently, to pseudo-abscesses.

Salivary Glands and Pancreas.—The cells of the *salivary glands* and of the *pancreas* frequently show granular degeneration, and it is stated that these structures become enlarged and firmer in consistence than normal early in the disease. A suppurative inflammation of the parotid glands—parotid bubo—sometimes occurs as a complication of the disease.

The **Respiratory Organs** present various and important lesions. Ulcerative laryngitis not infrequently occurs. The situation of the ulcers may be in the posterior wall, upon the ary-epiglottidean folds, or at the base of the epiglottis. Acute laryngeal œdema occasionally results, and may necessitate the performance of tracheotomy. This operation was found necessary in 8 of the 20 cases noted in the statistics of the Pathological Institute of Munich. Bronchitis is common, and the bronchial tubes show those changes which underlie the various forms of bronchial catarrh in other diseases. The lungs show changes referable to the twofold condition of an enfeebled circulation and a blunted condition of the nervous system. Broncho-pneumonia in enteric fever, as in other so-called typhoid conditions attended by an obtunded condition of the nervous system and impairment of the laryngeal reflex, is nearly always due to the entrance into the upper air passages and bronchial tubes of septic particles from the mouth and pharynx, either by inhalation or during the act of deglutition. Such infection causes bronchial catarrh, which by extension involves the finer tubes and air-vesicles.

Hypostasis of the dependent portion of the lung and splenization are common. Many cases of so-called hypostatic congestion are regarded by Strümpell as being, in reality, instances of broncho-pneumonia. Other pulmonary lesions, more or less frequently encountered, are putrid bronchitis, gangrene, abscesses, and infarction. Croupous pneumonia is a frequent complication due to secondary infection by the *diplococcus pneumoniæ*, and is usually encountered after the course of the disease has become well established. Croupous pneumonia is, however, in some instances apparently due not to infection by the diplococcus pneumoniæ, but to infection by the bacillus of Eberth. Under these circumstances it usually occurs early in the course of the attack, and has been attributed to localization of the specific process. The difference between the two forms, however, is rather a bacteriological than an anatomical one. In a case of mine in the Jefferson Hospital, Coplin found Eberth's bacilli in the pulmonary exudate. Involvement of the pleura is not very common. Fibrinous pleurisy and empyema occur.

The central nervous system rarely shows gross lesions. Sometimes slight adhesions of the dura mater to the cranium are found. Increased vascularity of the pia with minute hemorrhages and vascular injection of the brain substance may occur early. When death takes place late in the course of the attack œdema and moderate distention of the ventricles are noted, and are to be attributed to wasting of the brain tissue. Very rarely large hemorrhages or the signs of a purulent meningitis are found. The lesions of peripheral neuritis have been frequently observed.

SYMPTOMS.—**General Clinical Course.**—The period of incubation of enteric fever is variable. In general it may be set down as from two to three weeks. The incubation period in some well-authenticated cases has not exceeded four or five days. In a case of my own in the Philadelphia Hospital it was, so far as could be determined, only four days. The onset is commonly so insidious that the patient is unable to designate the actual time of the beginning of the attack. Prodromal symptoms consist of general lassitude and languor, fatigue upon slight exertion, vertigo, headache, frontal, occipital, or general, but almost always aggravated toward evening; slight nausea, loss of appetite, and in some cases fleeting colicky pains in the abdomen. A tendency to diarrhœa is often present in the prodromal stage, or, if absent, is easily induced by the administration of mild laxatives.

The facies soon becomes dull, there is slight impairment of hearing, and the patient complains of aching of the back and limbs. The tongue is coated, and epistaxis, which may consist of only a few drops of blood, a mere stain upon the handkerchief, constitutes a sign of diagnostic importance at this period of the disease.

These prodromal symptoms, not well defined in every case, continue for a varying period, and in some instances last for a week or more; in others, however, where the infection is intense, characteristic symptoms of marked severity may develop within two or three days after the occurrence of the primary symptoms. In default of other definite criteria the actual onset of the disease is to be reckoned from the day the patient betakes himself to bed, but, as this event depends much upon individual temperament, some difficulty usually arises in estimating definitely the date of the beginning of the attack. The onset, however, is rarely abrupt, and is less frequently so in adults than in children; it is seldom marked by a decided rigor, but is in some instances attended by chilly sensations.

The *first week* of the disease is characterized by a gradual rise in temperature, the subfebrile temperature of the prodromal stage gradually merging into the steadily increasing fever of the first week. The record of each evening's temperature exceeds that of the previous evening by a degree or a degree and a half of the Fahrenheit scale, until by the evening of the fifth day it reaches 103° or 104° F.

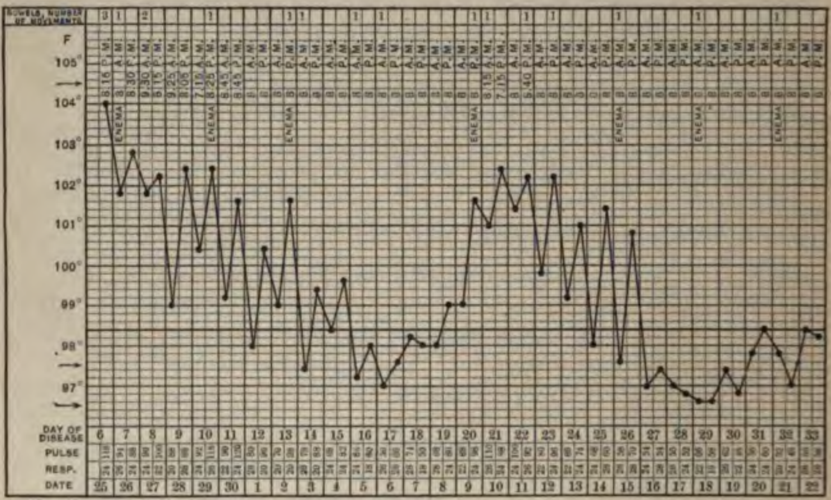
About this time the temperature commonly attains the fastigium, the elevation which, in the absence of complications, it is to maintain during the course of the attack.

The pulse is increased in frequency, and although the volume is full the tension is low; it after a time becomes dicrotic. The skin is usually hot and dry; exceptionally even at this period it is moist and bathed in perspiration. The headache of the prodromal stage increases in severity, and epistaxis, which may or may not have occurred during the prodromal period, is often present during the first week; it is usually slight, sometimes considerable. Muscular prostration is marked; the patient's expression is already dull and apathetic, although upon being aroused his mind is clear and his memory good.

Sleep is restless and often disturbed by disagreeable dreams, while toward the end of the first week slight transient delirium develops, especially upon awakening.

The lips are parched and dry, and the tongue, usually at this period moist, is swollen and covered with a whitish fur, thin or thick and creamy, and limited to the dorsum, the margins and tip being bright red. Appetite is lost, and there is thirst; diarrhœa continues, although in many cases the bowels are confined at the onset. Diarrhœa does not at this stage usually exceed four or five loose yellow stools in the course of twenty-four hours, fecal in character and unattended by pain. Diarrhœa may, however, be absent during the entire course of the disease. Toward the end of the first week tympanites develops, and there is tenderness elicited by pressure in the ileo-cæcal region or in the neighborhood of the umbilicus; gurgling may also be developed by pressure in the right iliac region. Toward the end of the first week an increase in the area of splenic dulness may be detected, and the characteristic rash appears as rose colored spots. The urine is diminished in quantity, its urea increased, and the chlorides diminished, while frequently a trace of albumin is present. At this period a few scattered râles may be heard over both sides of the chest posteriorly, especially

FIG. 11.



Enteric fever, single relapse (Pennsylvania Hospital).

at the bases, and slight occasional cough may occur as a symptom of bronchitis almost from the very onset.

There is usually pallor of the face, with circumscribed flushing of the cheeks; the conjunctivæ are pale and the pupils considerably dilated.

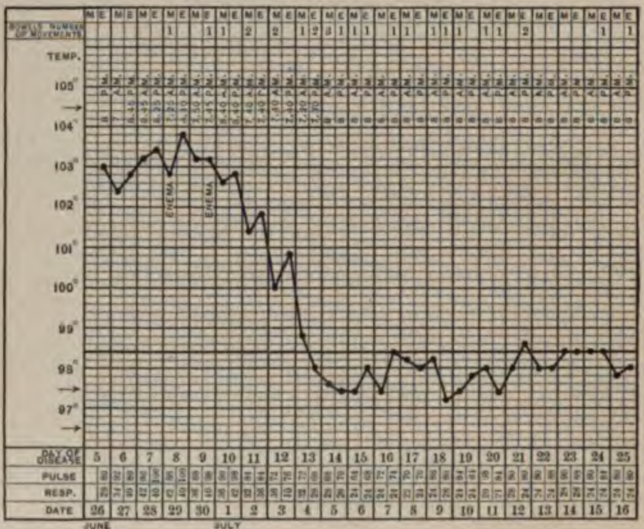
In the *second week* the symptoms are aggravated; the fever remains high and is continuous or subcontinuous in type. The action of the heart is feeble and the first sound weak; the pulse varies in frequency from 90 to 120, is less full than during the first week, and may become less dicrotic. The expression is duller, the flush upon the cheeks deepens, and in severe cases the face becomes slightly dusky. The headache now spontaneously diminishes. The patient becomes dull and somnolent, but has little or no sound sleep; he is indifferent and apathetic, and the dulness of hearing increases. When aroused and questioned he commonly replies connectedly, but usually in monosyllables. Muscular movements are feeble and tremulous; the tongue is dry, red, and fissured, often incrusted with sordes and protruded with difficulty. The patient lies upon his back, with his eyes half closed, listless, and making feeble, wandering movements with his hands. The delirium is usually wandering or muttering in character, and if the case be severe there may be involuntary discharges of the urine and fæces, or the urine may be retained. In other cases delirium is active, even maniacal, and this variety may develop suddenly from the wandering form. Tympanites, diarrhœa, and other abdominal symptoms are more marked; fresh crops of the rash continue to make their appearance, and evidences of pulmonary congestion become decided. In favorable cases defervescence may now set in.

In the *third week* the symptoms are the same, but more grave. The loss of strength is extreme and the emaciation marked; the muscles are flabby and the cheeks hollow. The pulse is feeble and accelerated, and sometimes running in character; the rash continues to reappear in fresh crops; free sweating is common and sudamina appear, especially upon the abdomen and lower portion of the thorax. Muscular movements are tremulous and ataxic, and subsultus tendinum may occur. Bed-sores may now make their appearance, and there is danger of pulmonary complications and failure of the circulation. The heart's action is feeble, the impulse faint or imperceptible, and the first sound frequently inaudible. The temperature early in the third week usually conforms to the remittent type.

With the *fourth week* the temperature range becomes intermittent. This period may mark, even in grave attacks, the beginning of convalescence. In that case the morning remissions of temperature for a few days often reach subnormal ranges. The symptoms ameliorate, gradual improvement takes place, the tongue cleans, constipation replaces diarrhœa, the area of splenic dulness decreases, the urine becomes clear and more abundant, and albumin, if present, disappears; the skin is now bathed in perspiration; emaciation, however, does not stop until the temperature falls to normal; a ravenous hunger now develops, and is characteristic of the period. Convalescence is tardy, and is apt to be protracted by complications, sequels, or relapses. The temperature is at this time extremely unstable, and recrudescences of fever are brought about by slight causes.

Special Symptoms.—**Temperature.**—In uncomplicated cases the temperature range may be divided into four periods, each of which has its special fever curve, the time covered by each period usually being one week, but often only five days, and exceptionally eight or nine days. This typical temperature curve is modified by complications and treatment and prolonged by relapses and sequels. In the stage of onset or during the first week of the disease the temperature steadily rises until about the fifth or sixth day, the temperature of each evening being higher than that of the preceding evening, and the temperature of each morning higher than that of the preceding morning: while this step-like rise, as it has been called, occurs in many cases, it must not be regarded as invariable. In this way, by the end of the first week a temperature of 104° or 105° F. may be reached, and the height of the temperature range established. This fever range, the acme or fastigium, indicates the probable range of temperature in the absence of complications throughout the course of the case. Thus, if the temperature range be high upon the fifth or sixth day, the case is likely to prove one characterized by severe pyrexia; on the other hand, if at this period the fever be of moderate degree, the case is likely to pursue a mild febrile course. After the fastigium is attained, and during the course of the second week, the temperature becomes subcontinuous in type, the variations between the morning remissions and evening exacerbations corresponding to the diurnal variations of the normal temperature. Toward the end of the second week or at the beginning of the third week marked variations between the morning and evening temperatures usually occur, and the fever curve becomes distinctly remittent in type, the extent of the remissions being, at times, as much as three or four degrees. It is at this period of the disease that free sweating with sudamina is apt

Fig. 12.

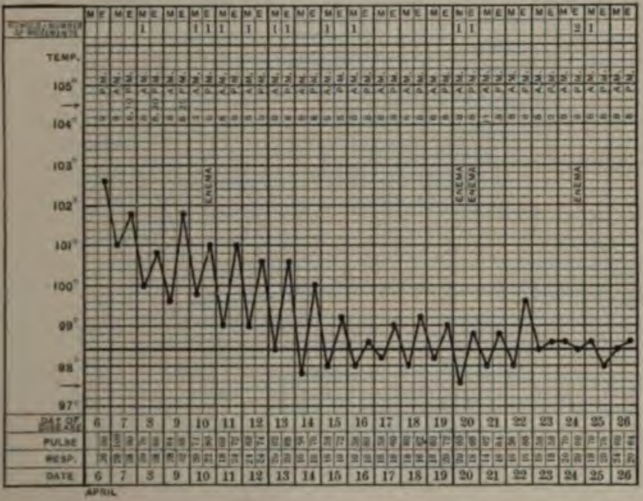


Abortive form of enteric fever, complete defervescence on the 13th day (Pennsylvania Hospital).

to occur. With the decline of the febrile process the temperature range assumes at the end of the third week or during the fourth week an intermittent type. At this period, while the evening temperature may show a marked febrile rise, the morning temperature is normal or even below normal. The evening temperature upon each succeeding day shows a progressively diminished rise, until the range of health is reached, the establishment of convalescence not taking place until the evening temperature ceases to rise above the normal.

Departures from the type of the fever curve frequently occur. In some cases, instead of the gradual rise in the temperature characterizing the first week of the disease, an abrupt rise takes place, and it is in this class of cases especially that the onset of the disease is accompanied by a chill or chilliness. Again, the defervescence, instead of occurring during the fourth week and occupying several days, may set in very much earlier and be much shorter in duration, the temperature declining by a rapid lysis, exceptionally by crisis—*the abortive form.* In a group of cases in which the clinical phenomena are well marked the fever terminates by a gradual fall during the course of the second or early in the third week—*typhus levissimus.* These aberrant forms of the temperature curve are rare. Still more rare are cases characterized by an inverse temperature, the morning temperature being for some days or occasionally higher than that of the evening, in the absence of complications. It is, however, very common for the temperature curve to be interrupted by intercurrent diseases; thus, if pulmonary complications occur the temperature may assume a higher range and its course be protracted and irregular. As a rule, the temperature range corresponds to the intensity of the infective process, and when a high temperature is continuously maintained the prognosis must be regarded

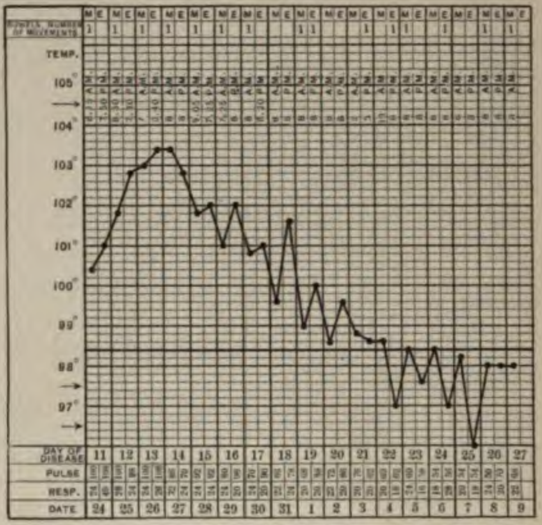
FIG. 13.



Mild enteric fever, *Typhus levissimus* (Pennsylvania Hospital).

as unfavorable. The converse of this statement is, however, not to be assumed, since grave, even fatal, cases occasionally occur in which the temperature does not rise above 102°–103° F. during the whole course of the attack. ✓A sudden drop in the temperature, especially when occurring in the course of the second or third week of the attack, must be regarded with anxiety, as it usually indicates the presence of some serious complication. Thus intestinal hemorrhage is almost always attended by a sudden fall in temperature, often of several degrees, and frequently before the blood makes its appearance in the discharges from the bowel. The same phenomenon, accompanied by symptoms of shock, may also attend the occurrence of intestinal perforation, and the onset of croupous pneumonia as a complication of enteric fever is occasionally attended by a brief fall in temperature. Very high temperature, so common in typhus fever, relapsing fever, and in other acute infectious diseases, observed as an early manifestation, is to be regarded as an evidence of intense infection or of the occurrence of an early complication. Hyperpyrexia may occur as a preagonistic phenomenon.

Fig. 14.

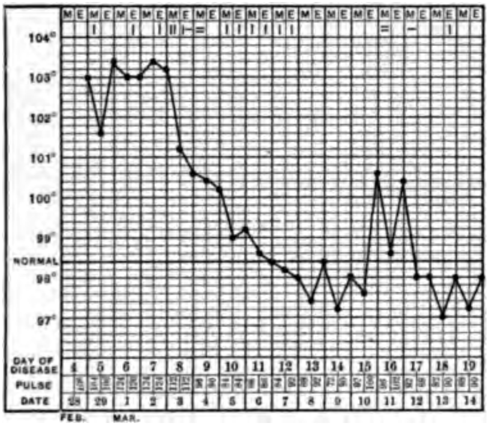


Enteric fever, subnormal temperature after defervescence (Pennsylvania Hospital).

During convalescence the temperature for the first few days frequently remains below normal. Its chief characteristic, however, at this period, is its instability, its liability to be disturbed by trifling causes. Thus, even after the temperature has been normal for a number of days rises may take place as the result of dietary errors, constipation, the visits of friends, emotional disturbances, and like simple causes. Such recrudescences of fever commonly last some hours, very rarely more than a day or two. As recrudescences sometimes follow the first taking of solid food, this brief fever of convalescence has been called *febris carnis*. In other instances after the establishment of convalescence the temperature continues to range at subfebrile levels—

100°-101° F. This bed-fever, as it has been termed, is to be ascribed to the influence upon an unstable temperature of the retention within the body of the products of waste, the elimination of which has been interfered with by the inactivity of the skin and the constipation characterizing early convalescence. So soon as the patient is allowed to be out of bed constipation usually ceases, the skin becomes more active, and elimination in general more effective. Under these influences the subfebrile temperature rapidly falls to normal. Cases of enteric fever pursuing an afebrile course, although the disease possesses otherwise characteristic features, have been described. This must be regarded as a very rare form of the disease. Such cases are certainly almost unknown in this country.

FIG. 15.



Enteric fever, mild case: normal temperature 11th day; recrudescence 15th day, due to constipation, and terminating after movement of bowels on the 17th day (German Hospital).

The temperature range of the relapse usually corresponds to that of the original attack; the fastigium is, however, more quickly attained and defervescence occurs earlier.

Circulatory System.—The pulse-frequency corresponds to the intensity of the fever, but not so closely as is usual in febrile diseases. Enteric fever is a fever of relatively slow pulse. Its frequency is extremely susceptible to variations, and may be greatly modified by slight causes, such as change in posture or movements in bed. In severe cases it becomes irregular in rhythm and force—phenomena of unfavorable prognostic import. In the first week the volume of the pulse is full, but its tension low, and at this period the pulse is frequently already dicrotic. Dicrotism is important from a diagnostic standpoint; it is rarer in childhood than in adult life. During the first week the pulse is usually though not invariably above 100, but later, in severe cases, it may become greatly accelerated and very weak. Coldness of the extremities and lividity of the surface are also indications of enfeebled circulation, and, as collapse may develop from this condition, are always to be regarded as symptoms of immediate gravity.

With the onset of convalescence the pulse gradually returns to normal. Its frequency is usually accelerated, but a slow pulse is not uncommon, and instances of a fall so low as forty or even thirty beats to the minute are occasionally observed (bradycardia).

The heart's action in mild cases and during the early period of the disease is but little disturbed, but in severe cases the force of the impulse progressively diminishes until, toward the close of the second week, it becomes extremely feeble or almost imperceptible, and the first sound very faint or inaudible. Occasionally there develops a faint systolic bruit at the apex. Pericarditis and endocarditis are of rare occurrence. Myocarditis, however, is more frequent, and the cardiac weakness shown in the feeble impulse and faint first sound is due in part at least to degenerative changes taking place in the myocardium, and in part to functional disturbance of the nervous system. Under these circumstances sudden death may take place as a result of cardiac failure. Slight œdema of the ankles, dependent upon cardiac weakness and anæmia, may occur in early convalescence.

The blood has been carefully studied by Thayer,[1] who found the number of red corpuscles at the beginning of the fever usually normal. During the first weeks the number of corpuscles falls gradually, but to a relatively slight extent. The fall is more rapid upon defervescence, reaching its lowest point about the first week of convalescence. Recovery from this anæmia is gradual. As a rule, the decrease in the number of red corpuscles bears direct relation to the severity of the case, but grave anæmia may follow cases that appear to be mild. Severe post-typhoid anæmia may constitute a grave sequel of the attack.

The hæmoglobin diminishes with the red corpuscles and to a greater proportionate extent. Its return to the normal is less rapid. The leucocytes are at the beginning about normal, but their number gradually falls, reaching the lowest point about the end of defervescence. The diminution is slight; the return to normal is gradual. The absence of leucocytosis may in a suspected case be of diagnostic value.

Venous thrombosis, especially affecting the veins of the lower extremities, and most frequently a crural vein, occurs in about 1 per cent. of the cases. Its time of occurrence is usually late in the course of the disease or during convalescence. It is manifested by rapidly oncoming œdema of the extremity, with pain. The acute phenomena usually subside in the course of a few weeks; permanent œdema with difficulty in walking often results. It sometimes happens that a portion of the thrombus becomes dislodged. The left crural vein is more frequently involved than the right.

Respiratory System.—The frequency of the respiratory movements varies with the intensity of the febrile process. Pulmonary symptoms are among the most frequent and important manifestations accompanying enteric fever, although for the most part they are to be regarded as complications rather than as direct results of the specific infection.

Bronchitis is very common. It is usually an early manifestation, and therefore may have diagnostic importance. Its existence is revealed by râles, usually at first dry and scattered. In cases of moderate severity the bronchitis has no important bearing upon the course of the disease; in the graver cases it often extends to the finer tubes.

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[1] *Johns Hopkins Hospital Reports*, vol. iv. No. 1.

Broncho-pneumonia may develop in enteric fever, as in other diseases attended by great prostration of the nervous system, as an inhalation or deglutition pneumonia. Hypostatic congestion and œdema in the later periods of the disease are common, and are to be ascribed to enfeeblement of the circulation and the lowered tone of the nervous system. Strümpell is inclined to look upon many of the instances usually regarded as cases of hypostatic congestion as in reality broncho-pneumonia. The physical signs are impairment of resonance at the bases posteriorly, feeble and distant respiratory murmur, and fine, moist râles, chiefly inspiratory.

Croupous pneumonia may occur as a complication of enteric fever, usually in the second and third weeks. In the majority of instances it is to be regarded as a true complication dependent upon a secondary infection with the pneumococcus. It may be overlooked unless the chest be systematically examined, as the subjective symptoms are not marked. Croupous pneumonia may develop early, the onset of the affection being abrupt, with a chill, and the pulmonary phenomena so dominating the clinical picture as to obscure the signs of enteric fever. After the first week, however, intestinal phenomena, enlargement of the spleen, rose spots, and the subsidence of lung symptoms enable the diagnosis of enteric fever to be made. In such cases, known as pneumo-typhus, the pulmonary lesion is probably due not to infection by the pneumococcus, but to an early pulmonary localization of Eberth's bacillus.

Pleurisy occasionally occurs as a complication of enteric fever.

Catarrhal laryngitis is sometimes met with, and laryngeal perichondritis, with or without accompanying ulceration, may occur, the lesions usually involving the posterior wall or the base of the epiglottis. Œdema is liable to occur in association with ulceration or perichondritis.

Epistaxis is a common symptom. It may appear in any period of the disease. It is commonly slight, but profuse, even serious, nose bleeding may occur. Strümpell mentions a case in which a fatal issue resulted. Very commonly during the period of prodromes, and often during the course of the disease, it amounts to nothing more than a stain upon the handkerchief caused by picking at the nostrils. Ulceration of the nasal mucous membrane is occasionally seen, and the fact that the nasal septum may be perforated or necrosis of the cartilages may follow with resulting deformities should be borne in mind, lest subsequently the lesions may in any case give rise to the suspicion that the patient has had syphilis.

Digestive System.—Marked disturbance of the digestive system occurs, and symptoms referable to the gastro-intestinal tract very often for a time dominate the clinical picture, while those dependent upon the general constitutional infection assume a subordinate rôle.

Anorexia, as a rule, occurs early and is complete. It usually persists until defervescence. At this time, however, hunger is often urgent. Thirst is a prominent symptom, and even when the patient's mental condition becomes such that he fails to demand fluids, he drinks them with avidity when proffered.

The *tongue* early in the course of the attack is moist, swollen, and usually covered with a whitish fur; later, the coating clears off from the edges and tip, which are often of a bright red color. The tongue may remain moist throughout, but in severe cases it soon becomes dry and is covered with a dark brown coating with numerous cracks and fissures. Such a tongue may bleed, and this, together with oozing from the gums, leads to the accumulation upon the teeth, lips, and gums of a collection of material consisting of clotted blood, retained food, and cast-off epithelium, to which the name of sordes is given. This condition may be to a large extent averted by careful and systematic cleansing of the mouth. The tongue cleans off upon the occurrence of convalescence.

The *lips* are cracked and dry, and the buccal mucous membrane dry and sticky.

The *pharynx* is not infrequently the seat of a catarrhal inflammation. Membranous pharyngitis occurs in rare cases and is of serious import: the false membrane may extend into the œsophagus.

Faucial angina, occurring coincidently with a diffused erythema upon the surface of the body, as happens in a small proportion of the cases, may give rise to a suspicion of scarlet fever.

From the pharynx, by extension of the infection through the Eustachian tubes, the middle ear may become involved, and suppurative *otitis media* take place with perforation of the tympanum. This condition may, owing to the patient's mental condition, be overlooked. Not infrequently, and usually in the third week of the disease, parotitis—parotid bubo—develops in consequence of infection by way of the duct of Steno. This, though usually unilateral, may involve both glands. Its usual termination is by suppuration, and its occurrence adds greatly to the gravity of the prognosis. Inflammation of the middle ear and of the parotid gland is the result of secondary infection.

Nausea and vomiting occasionally occur early in the disease. They are much more common as manifestations of enteric fever during childhood than during adult life. Repeated vomiting is a serious symptom and of unfavorable import, since it is, as a rule, to be ascribed to a complication, such as nephritis, a cerebral lesion, or developing peritonitis. Vomiting under these circumstances does not occur early, but is a late manifestation of the disease. In certain rare instances vomiting is so persistent that death from exhaustion may ensue, and in some of the cases ulceration of the stomach has been found after death.

Symptoms referable to the intestinal tract are constant. In the early days of the disease constipation is the rule, and in not a few cases this condition continues throughout the entire course of the attack. The diarrhœa is usually proportionate to the severity of the attack and to the extent of the local intestinal lesions. This is not, however, invariably the case. Even extensive lesions of the glands of the small intestine may be present, while the colon contains solid fæces.

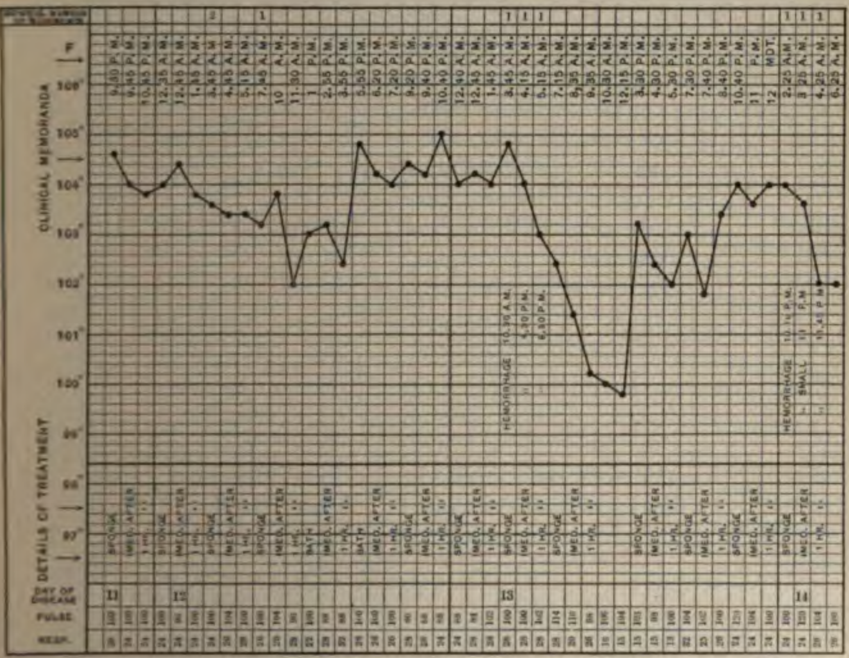
Diarrhœa is common toward the end of the first and during the course of the second week. It may not, however, occur until toward the close of the attack. It is to be ascribed in part to the local ulceration, but is chiefly due to the accompanying intestinal catarrh, especially to catarrh of the large intestine. The number of stools in the course of twenty-four hours varies from four or six to fifteen or twenty. They are usually copious, in odor offensive, in consistency thin, in color yellowish or ochre yellow, sometimes greenish, in reaction alkaline, and are voided without pain. They frequently contain milk curds, and later in the course of the attack shreds of necrotic tissue from the sloughs. Microscopically, the stools contain fragments of food, large numbers of crystals of triple phosphate, epithelia, and various bacteria. The bacillus of Eberth is not usually found in the intestinal discharges earlier than the tenth day, frequently not until the sixteenth day.

Tympanites is common. It usually occurs during the second week. It is, as a rule, slight, but may be excessive. Great abdominal distention is sometimes associated with deep ulceration, and must always be regarded as of unfavorable prognostic import.

Abdominal tenderness may be elicited upon gentle pressure in the majority of the cases. Its most common seat is in the right iliac fossa; sometimes it is restricted to the neighborhood of the umbilicus; rarely it is general. Pressure in the right iliac fossa very often elicits gurgling—a sign of minor importance from the standpoint of diagnosis, since it is present in many other conditions.

Spontaneous abdominal pain is not common in enteric fever. It may, however, arise in consequence of extensive or deep ulceration, and is present in local peritonitis.

FIG. 16.



Rapid fall of temperature due to hemorrhage on the 13th day of the attack (Pennsylvania Hospital).

Intestinal hemorrhage occurs in 3 to 5 per cent. of all cases. It must always be regarded as a serious complication. It usually appears at the time of the separation of the sloughs, toward the end of the second and during the third week of the attack. The cases are, as a rule, otherwise serious, and the bleeding, even when slight, should be regarded with anxiety, as constituting an additional element of danger. The amount of blood varies from a slight trace in the stools to a copious evacuation of bright red blood. Death may occur from rapid blood loss. There are cases in which hemorrhage takes place into the bowel without the blood at once appearing in the stools—concealed hemorrhage. The symptoms of internal bleeding are present, and after a time blood appears in the stools, usually in dark clots. The occurrence of hemorrhage is manifested by an abrupt fall of the temperature, amounting to several degrees, sometimes eight or ten degrees of Fahrenheit's scale. This decline of temperature is very often attended by temporary amelioration of the symptoms, especially those relating to the nervous system. Thus, if, as frequently happens, in the second or third week of the disease the patient is delirious, somnolent, or stuporose, or even comatose, and with subsultus tendinum, ataxic muscular movements, and grasping at invisible objects in the air, the occurrence of a hemorrhage from the bowels may be followed by a striking change. The delirium disappears, consciousness may be regained, and the ataxic phenomena cease. If, however, the loss of blood be large, the pulse becomes rapid and feeble, coldness of the extremities occurs, there are sensations of faintness, great prostration, pallor, and frequently death may follow in collapse. If the patient rallies, the temperature rises again and the disease resumes its regular course, with a reappearance of the nervous symptoms. In concealed hemorrhage the blood may not make its appearance in the stools for some time, even a day or two, after the occurrence of the hemorrhage. In these cases the diagnosis of hemorrhage is made by the sudden fall of the temperature, amounting to several degrees, rapid and feeble pulse, pallor and faintness, great prostration, amelioration of the nervous symptoms, and tendency to collapse. Further, an examination of the abdomen reveals upon palpation a sensation of resistance or a doughy feeling in the neighborhood of the right iliac fossa and frequently extending up along the line of the ascending colon, and percussion over the same area yields an area of dulness in a region of the abdomen previously and usually tympanitic. Later, usually with the next evacuation from the bowels, evidences of bleeding in the form of large dark clots are found, the evacuation of which is commonly followed by the reappearance of the tympanitic percussion sound over the right iliac region. It occasionally happens that the amelioration of the general symptoms occurring after moderate hemorrhage from the bowels persists, and this accident marks the beginning of convalescence. Some observers have gone so far as to regard hemorrhage as not in itself a very dangerous occurrence. Modern statistics show that from 30 to 50 per cent. of cases in which hemorrhage takes place die in consequence of exhaustion supervening upon uncontrollable bleeding or from subsequent perforation and peritonitis. Hemorrhage occurs with such frequency that we may almost consider it a symptom, rather than a complication, of the graver forms of the disease.

Perforation of the intestinal wall, with extravasation of the intestinal contents into the peritoneal cavity, constitutes the most serious complication of the disease. It occurs in about 11 per cent. of the fatal cases, and is a cause of death in about 2 or 3 per cent. of all cases: it is more common in males than in females, and is extremely rare in childhood and in the aged, not often occurring after the fortieth year. I have, however, seen double perforation of the bowel in a man over fifty years of age. It is more apt to occur in cases otherwise severe than in mild cases, and especially in those cases marked by profuse diarrhœa, large tympanites, and great abdominal tenderness, and is often preceded by hemorrhage. It is more frequent in the third and fourth weeks, but is liable to occur during the second week, and may appear as late as the ninth or tenth week. The situation of the perforation is usually the lower part of the ileum, but it may be in the caput coli or in the appendix. It is immediately followed by an acute septic peritonitis, almost always diffuse, although in rare instances localized by the immediate formation of adhesions to an adjacent loop of gut, or other viscus. Death may result immediately from shock. Usually the occurrence of perforation is manifested by intense pain in the abdomen, commencing in the neighborhood of the right iliac fossa, and, as peritonitis develops, extending over the entire surface of the abdomen; symptoms of collapse, characterized by subnormal temperature, shallow, feeble breathing, cold clammy sweats, a feeble running pulse, great thirst, frequent vomiting, and partial suppression of urine. If death do not then occur, symptoms of peritonitis devolop; the temperature again rises, the abdomen becomes extremely tympanitic, and the lower segment of the liver dulness is effaced—a very important diagnostic sign as indicating the escape of the gases from the intestines, through the perforation, into the abdominal cavity; the abdominal walls become rigid, tenderness is extreme, and the legs are drawn up; vomiting sets in, the pulse becomes rapid, small, and thready, and the physiognomy that of intense suffering. Death takes place in the course of from two to four days, exceptionally later. Peritonitis, local or diffuse, may originate without actual perforation by extension of inflammation at the seat of ulceration from the mucous to the serous coat of the intestine, the latter structure remaining intact so far as perforation is concerned. It may also be caused by the rupture of a pseudo-abscess following softening of a mesenteric gland, and occasionally as a result of the bursting of abscesses of other structures, as of the liver, gall bladder, spleen, or the abdominal wall.

Splenic enlargement, according to Leube, occurs in over 90 per cent. of the cases of enteric fever: it is first detected toward the end of the first week, coincidently with the appearance of the rash, and continues to increase in size until about the fourteenth day. With the beginning of the fourth week—*i. e.* with defervescence—a diminution of volume takes place. Splenic enlargement persisting after the establishment of convalescence should be regarded with suspicion as indicating the possibility of a relapse. Usually the large spleen can be felt below the costal margin, but if the colon be greatly distended with gas it may be so pushed back that even the normal area of dulness cannot be made out for the surrounding tympany. It should also be remembered that enteric fever in the aged is frequently unaccompanied by an increase in the size of the spleen. Accidental rupture of the organ, as from a blow or from undue force in efforts at palpation, has been observed; spontaneous rupture is uncommon.

Jaundice is not frequently present in enteric fever, and symptoms referable to the liver are uncommon. Occasionally the organ is somewhat enlarged, but the parenchymatous degeneration gives rise to no clinical manifestations.

Nervous System.—Morbid phenomena relating to the nervous system are very common and diverse in enteric fever. Not rarely they dominate the clinical picture.

Headache is frequent, both in children and in adults; it is an early symptom, appearing during the period of prodromes and may vary in intensity from a dull supraorbital pain to a severe neuralgic and persistent headache. It is usually most severe in the frontal region, and, at least early in the course of the disease, becomes aggravated toward evening. So intense may be the headache that it sometimes suggests meningitis, especially if, as sometimes happens, it is associated with vomiting, muscular twitchings, and retraction of the neck. It usually ceases spontaneously about the middle of the second week, and very often gives place to mild delirium. Headache may be associated with or alternate with *somnolence* and *apathy*. On the other hand, distressing wakefulness may be present during the early course of the disease. In a majority of the cases, under expectant methods of treatment, the patient's mental condition as the attack advances is peculiar: he is drowsy, dull, and apathetic, and indifferent to his surroundings. The hebetude may be so marked that drink, though partaken of eagerly when offered, is not asked for during long periods. The patient pays little heed to his surroundings and rarely volunteers a remark. When aroused, however, he replies to questions intelligently, but slowly and in monosyllables, and almost immediately falls again into a somnolent state. An evidence of the extreme apathy of the patient's mental state is observed in the manner in which he responds to the request to put out his tongue: the organ is protruded slowly, and only in response to several sharp requests; it is often not retracted at once, but held out until the order to put it in again is given.

In some instances hebetude is present from the early days of the attack; in others the mind remains clear throughout the whole course of the sickness. The latter condition is the rule in cases treated by systematic cold bathing, which also favorably modifies delirium and other nervous symptoms.

Delirium is present in a majority of the cases. As a rule, it does not commence before the middle of the second week, about the period when the headache subsides. In a small proportion of the cases it does not appear until late in the course of the disease, and lasts only a few days. In rare cases maniacal delirium occurs at the beginning of the attack and may be the first symptom to attract the attention of the friends of the patient.

The character of the delirium varies greatly. It is often slight and occasional, occurring chiefly in the night-time or on waking from sleep in patients who are at other times entirely rational. More commonly it is continuous, and usually of a quiet form. It may be—though this is not common—active and noisy, passing as prostration becomes more marked into the low, muttering form known as typho-mania, or into a wandering, fatuous state with trembling like that of alcoholism. The last form is common in heavy drinkers. The delirium of enteric fever is often accompanied with suicidal impulses, and the patient should never after delirium has appeared be left alone. In the graver cases delirium gradually gives way to unconsciousness. The patient can be roused with difficulty or not at all. Urine is retained, or both urine and fæces are voided unconsciously. The lips are tremulous; there is twitching of the fingers and hands; subsultus tendinum and picking at the bed clothing or grasping at invisible objects in the air—carphologia. Sometimes the condition known as coma-vigil develops: the patient's eyes are open and he appears to see, or even to follow the movements of his attendants; he mutters indistinctly, but he is unconscious and oblivious. These are symptoms of the gravest import.

The well-known tendency of delirium to take its form from the intellectual development and mental habit of the individual in sickness of every kind serves to explain the fact that in enteric fever in childhood apathy, somnolence, and stupor are much more common than active or even wandering delirium.

Convulsions are rare. The onset of the attack is gradual in children as in adults, and the convulsions so common at the beginning of the other acute infections do not occur.

Muscular weakness is marked in all cases and progresses with the disease. Many patients are, however, able to assist themselves, to sit up in bed, or even to rise to stool during the whole course of the attack. In the milder cases the patients, though very weak, are often able to go about, and it is not uncommon for walking cases to present themselves at the out-patient services of hospitals in the second or third week of the attack. In grave cases muscular debility is complete. In such cases, if recovery take place, there is some œdema of the legs and ankles during convalescence.

Tremor is present in many of the severer cases. The tongue trembles as it is protruded, the lips quiver, and the movements of the hands are trembling and uncertain. This phenomenon is more common in those addicted to alcohol and in aged persons. More rarely it may occur in young and temperate persons, and it is occasionally observed in cases in which there is no impairment of the mental faculties. Rigid contractions of groups of muscles of the neck, trunk, or extremities are met with in rare instances, and, as a rule, in females. The knee jerks and the cutaneous reflexes are slightly increased. In deeply soporose conditions they may be enfeebled or absent altogether.

The organs of special sensation present symptoms that are important. *Deafness* is very common. As a symptom it affects both ears, and is of nervous origin. It appears toward the end of the first or during the second week. As a complication middle-ear inflammation may cause one-sided deafness.

Vertigo sometimes occurs as an early symptom. Subjective auditory sensations, ringing and humming, often annoy patients during the early days of the attack.

Dilatation of the pupils occurs in at least three-fourths of the cases. It is apt to come on during the second week, together with the delirium.

It is often present, however, when there is no delirium or other marked nervous phenomenon. The pupils are not widely dilated, and respond slowly to the stimulus of light. In comatose cases the pupils may be contracted. Injection of the bloodvessels of the conjunctiva is rare.

Neuralgias, chiefly trigeminal and intercostal, occur during convalescence.

Cutaneous hyperæsthesia is common in children and women. It may occur during the course of the attack or not until convalescence. It is, as a rule, restricted to the abdomen and the lower extremities. It is often associated with rhachialgia, and points of spinal tenderness.

Localized tenderness of muscles may be encountered. It is probably due to myositis.

Neuritis may occur during the course of the attack or as a sequel. Local neuritis may affect an arm or leg. There is great pain upon movement, tenderness in the line of the nerve-trunk and of the muscles. If the extremities are involved, wrist-drop or foot-drop may result.

The burning pains in the feet and ankles and the tenderness of the toes without sweating or discoloration, occasionally present during convalescence, are manifestations of local neuritis. These painful phenomena, as a rule, pass away in the course of two or three weeks; exceptionally they persist for several weeks. Multiple neuritis may affect the upper and lower limbs or the legs alone. The paraplegic type is much the most common. Recovery takes place very slowly, but is, in most of the cases, ultimately complete.

Aphasia, without hemiplegia, may occur; it is more common in children than in adults.

Insanity may develop after the defervescence—post-febrile insanity. It terminates, as a rule, in recovery in the course of some weeks or months.

The Urinary System.—The urine presents the physical and chemical changes observed in the other acute infectious diseases. It is diminished in quantity during the first and second weeks. Notwithstanding the increased amount of fluid consumed by the patient, the urine excreted may not exceed one half or even one fourth the normal quantity. In many cases it is diminished until convalescence, when it becomes, as a general rule, copious and of low specific gravity. Its color is at first darker than in health. In the advanced stages of the disease and during convalescence it is pale. Modifications of the odor take place which are difficult to describe and are probably not constant. According to Robin, it is more aromatic than normal at the beginning, ammoniacal or even fetid toward the close of the attack, and regains its normal character during convalescence. The reaction is, as a rule, acid throughout the attack. At its close, however, the acid reaction becomes less intense, and in some instances it is feebly alkaline. The specific gravity in the early periods ranges from 1020 to 1030. After the close of the second week in some instances, and almost invariably during convalescence, the specific gravity falls to a point considerably below the normal. The abundant, limpid urine of early convalescence has occasionally a specific gravity as low as 1010. The quantity of urea present in the urine has been the subject of much discussion. Some observers have found it invariably increased during the early course of the disease; others have found it diminished. The uric acid is always increased. During the latter part of the attack, however, the amount falls to normal, and during convalescence it is less than in health. Copious deposits of the urates may occur at any time in the course of the disease. They are not critical and are without prognostic value. The chlorides are greatly diminished. Sometimes they do not exceed a mere trace. This diminution in the chlorides cannot be wholly explained either by the diminished amount ingested or by the increased amount voided in the stools. With the advent of convalescence the chlorides are greatly increased.

The Diazo-reaction.—Ehrlich in 1882 described a test which is in doubtful cases of diagnostic value. The reaction consists of a peculiar color developed in the urine and foam by the action of diazo-benzine-sulphonic acid in presence of an excess of ammonia. Two solutions are employed: (1) A 5 per cent. solution of sulphanilic acid, and (2) a $\frac{1}{2}$ per cent. solution of sodium nitrate. To make the test 40 c.c. of the first and 1 c.c. of the second are mixed together. Equal parts of this mixed solution and the urine are shaken together in a test-tube. Strong solution of the ammonia is then allowed to flow down the side of the tube. The reaction consists of the development at the junction of the ammonia with the fluid of a dark garnet or cherry-red ring. Upon brisk shaking a uniform red color is imparted to the fluid, while a delicate pink tinge is seen upon the foam. After standing for some hours an olive green precipitate is deposited. With normal urine the red color is lacking and the foam is brownish yellow. The diagnostic value of this test arises from the fact that the reaction occurs in the urine of the greater number of cases of enteric fever at some time during the course of the attack.

In 14 cases in which this reaction was studied in my last term of service in the wards of the Pennsylvania Hospital it was noted in 11, the examinations being made between the tenth and twenty-second days of the attack. In 15 additional cases in which the test was made later than the twenty-second day of the attack the response did not occur. The reaction occurs, however, in many other diseases, especially acute miliary tuberculosis, chronic tuberculosis, measles, scarlet fever, malarial fever, and pneumonia.

The *toxicity* of the urine is much increased. This increase is not dependent upon the elevation of temperature, and continues throughout the course of the fever and during convalescence. In cases systematically treated by cold bathing the elimination of toxins is increased, in some instances, according to Roque and Weill, to five or six times that of the normal.

Albuminuria is of frequent occurrence. The albumin in many cases amounts to a mere trace—febrile albuminuria. It may, however, be present in large amounts, together with tube casts and sometimes with blood, indicating the development of an acute nephritis. This complication may be so prominent as to merit consideration as a special variety of enteric fever—the renal form. These cases are always severe. In the majority of them recovery takes place, the symptoms of nephritis completely disappearing during or after convalescence. The signs of nephritis may not develop until after the fall of temperature—nephritis of convalescence.

Pus in the urine is not uncommon. It is sometimes associated with blood. Pyuria may be due to a pyelitis or to cystitis. **Blumer**[1] lated from ten cases the following bacteria, usually in pure culture: colon bacillus, the typhoid bacillus, the staphylococcus albus, an coccus that was not identified.

Retention of urine occurs in a considerable proportion of the ca Urethritis, cystitis, and orchitis may arise as the result of infec from catheters that have been improperly cared for.

The Skin.—The eruption appears, as a rule, between the seve and tenth days. Exceptionally it is met with as early as the fourt not discovered until as late as the twelfth day. In children it app somewhat earlier than in adults. It is not invariably present. Mur son states that the spots are more frequently absent in patients u ten and over thirty years of age than between ten and th years. There is no relation between the abundance of the rash and severity of the symptoms. The typhoid eruption is characteristic the disease, and when found establishes the diagnosis. It is mac papular, consisting of small, slightly elevated, rounded or oval iso spots of a rose pink color. Their diameter is from 1 to 4 millime They are indistinctly marginate, and alike to the eye and touch fai rounded and convex, but not acuminate, though a minute vesicle occasionally be discovered at their centre. They have been compa to flea-bites, from which, however, they differ in the absence of central mark and in their paler color. They disappear upon press and return immediately when the pressure is removed. They ma made to disappear and reappear under the eye by placing a finger u each side of a spot and making traction. As the skin becomes t they disappear; when it is relaxed they return. The exanthem developed in successive crops, each spot lasting three or four days leaving upon fading a faint patch of pigmentation. The spots ra appear after the middle of the third week. They are not found du convalescence, but reappear along with the other characteristic sympt of the disease upon the occurrence of relapse. The eruption is n present upon the dead body. The spots are most commonly pre upon the abdomen and lower part of the chest anteriorly. They frequently met with on the back, especially between the scapulæ, are occasionally present upon the upper part of the thigh. In s instances they are present upon the back alone, and in doubtful c should be sought for in this situation. The typhoid rash is in instances sparsely scattered over the arms and legs, and may be fo upon the face. The spots are usually few in number. It often hap that not more than six or eight can be discovered, and in many c the number present at one time does not much exceed a score. T are never confluent.

Erythema.—A scarlet rash, sometimes faint, sometimes bright occasionally observed during the course of the first week, especiall patients whose skin is fair and delicate. This rash is not very comm it is not peculiar to enteric fever, but is met with in other febrile af tions. If well marked, and particularly if it be associated with sl sore throat, as sometimes happens, the disease may be mistaken scarlet fever.

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[1] *Johns Hopkins Hospital Reports*, vol. v.

Urticaria occasionally occurs. *Herpes* also occurs, but is much less common in enteric fever than in some other febrile diseases. *Petechiæ* are rare. *Sudamina* appear at a later period of the disease, especially in cases in which there is profuse sweating. They consist of minute transparent vesicles scattered plentifully over the body, especially upon the abdomen. The *tache cérébrale*, as in other febrile diseases, can be readily produced. During the active febrile movement the skin is usually dry. The palms of the hands are dry and yellow in color. *Sweating* is, however, not rare; it is sometimes profuse and may be associated with chilliness. Slight *desquamation* is occasionally observed during convalescence, and changes occur in the nails, transverse, lustreless bands indicating the arrest of nutrition that has attended the course of the attack. The hair falls out, but after a time it grows again. The new hair is often lacking in lustre, but gradually acquires its normal appearance. Emaciation is usually great, often extreme.

Furuncles and abscesses of the skin occur during convalescence. They may be distributed on the back, buttocks, arms, and outer aspect of the thighs. Pustular eruptions sometimes occur. In 4 of a series of 71 cases occurring during a recent term of service in the Pennsylvania Hospital there appeared at the time of defervescence circumscribed groups of pustules symmetrically arranged on the inner side of both legs just below the knee.

Bed-sores may occur in the severer cases. Very often, but not invariably, they may be avoided by proper nursing.

Taches bleuâtres—spots of a delicate bluish or bluish gray tint, irregularly rounded form, from 4 to 12 millimetres in diameter, not raised above the surrounding surface nor affected by pressure—are met with in enteric fever and in some other diseases. The lesion is subcuticular. When present the individual spots are numerous and observed chiefly upon the abdomen, thighs, and legs. They appear to occur only upon the skin of patients who have body lice.

The *physiognomy* of persons ill of enteric fever is peculiar. In mild attacks there may be but little change of expression. More commonly the expression is dull, weary, the face pale, often with dusky flushing over one or both cheek bones. The dilatation of the pupils adds to the peculiarity of the facies.

Osseous System.—Inflammatory changes in the bones are not uncommon. Keen reported in 1876 an important series of cases of disease of the bones occurring after enteric fever. These cases occur frequently in childhood and adolescence. Of 41 cases studied by Murchison, the age of the patient was under twenty years in 19 cases, between twenty and thirty years in 11 cases, between thirty and forty years in 6 cases, and over forty years in 5 cases. The symptoms may first appear during the course of the attack, but are more common in convalescence. There is pain, at first vague, speedily becoming localized, usually severe, lancinating, aggravated at night. There is great local tenderness with tumefaction, with or without redness. After a time fluctuation appears, and one or more fistulous openings are formed which discharge a small quantity of pus. These sinuses frequently close spontaneously, to reopen in a short time. Some of the cases are due to streptococcus infection, most of them to infection by Eberth's bacilli.

Synovitis may occur. It is, however, a rare complication. As a rule, a single joint, exceptionally several joints, are implicated. Spontaneous dislocations are among the rare accidents of enteric fever. They are of the nature of "distention luxations," and are probably due to subacute synovitis with gradual serous distention of the capsular ligament.

INTERCURRENT AND CONCURRENT DISEASES.—Enteric fever during its course confers no immunity from other infectious processes. Erysipelas occurs as a rare complication, usually during convalescence. Scarlatina may precede, coexist with, or follow enteric fever. Taupin, Murchison, and others have reported instances in which patients suffering from scarlet fever have developed enteric fever, or in which scarlatina has developed during the course of enteric fever, and, again, instances in which the eruptions of the two diseases have coexisted. Measles may also develop during the course of enteric fever, either as an intercurrent malady or during convalescence.

Pertussis and varicella have been observed during the course of enteric fever. Diphtheria and pseudo-diphtheria occur with frequency in the course of enteric fever, especially in childhood. The false membrane may develop upon the pharynx, larynx, or on the mucous surface of the genitalia. Noma may also occur. This accident is apparently much more common in Europe than in this country. It is more liable to appear in childhood than in adult life. Tuberculous infection often occurs during or immediately after enteric fever, or the latter disease may call into activity a latent tuberculosis. Miliary tuberculosis or forms of pulmonary phthisis are sequels. Tuberculous meningitis and tuberculous ulceration of the intestine also occur as late sequels. Enteric fever frequently attacks those suffering from chronic diseases. I have on several occasions seen patients in the early stage of pulmonary consumption recover from an attack of enteric fever without intensification of the tuberculous process. In epilepsy it is unusual for the fits to occur, and choreic movements usually cease during an attack of enteric fever. The disappearance of sugar in the urine of diabetic patients during an attack of enteric fever may be in part at least accounted for by the character of the diet.

The term typho-malarial fever has been applied to two essentially different conditions. First, true typhoid fever occurring in persons recently subject to malarious influences or in malarious districts; and second, remittent fever. The term is an unfortunate one, and has given rise to no little confusion concerning the nosological conditions of the various forms of disease to which it has been applied.

W. Gilman Thompson has demonstrated by concurrent clinical data and microscopical examination of the blood the association in the same case of the typhoid and malarial infections[1] (Figs. 17–19, pp. 199, 200).

VARIETIES.—Enteric fever is a disease of complex symptomatology. The prominence of certain symptoms, the evidences of intense implication of special organs and modifications in the course of the disease, have led authors to describe numerous special forms. Thus, cases beginning with prominent symptoms of gastro-duodenal catarrh have been called *bilious*; those in which the nervous system is early and intensely involved have been regarded as *cerebro-spinal* forms. Early and severe implication of the kidneys has led to the classification of a certain group of cases under the head of *nephro-typhus*; the early manifestation of marked pulmonary symptoms, to the arrangement of another group of cases as *pneumo-typhus*, with pleurisy as *pleuro-typhus*, and where profuse sweating has occurred to the *sudoral* form. Others have sought to distinguish ataxic forms and adynamic forms and varieties based upon the prominence of particular symptoms. Such nosological arrangements are neither scientific nor convenient. Without attempting a closer analysis of the forms, the cases may be divided into typical and atypical. The former present the complexus of symptoms already described as constituting the clinical history of the disease, and further illustrated in the analysis of the symptoms and in the consideration of the complications and sequels. The atypical or imperfect forms constitute in most epidemics a large proportion of the cases. The following special forms require separate consideration:

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[1] *American Journal of the Medical Sciences*, August, 1894.

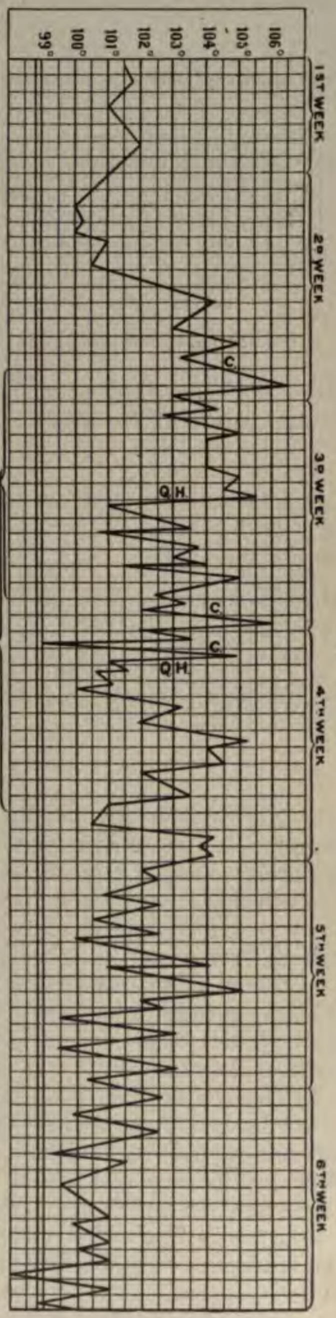


FIG. 17.

Dr. W. Gilman Thompson's case of malarial fever associated with enteric fever.

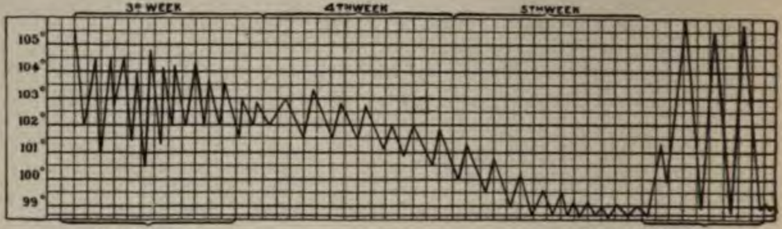
C. C. C. = chills. Hemorrhage from bowels. Very abundant malarial organisms. Q. H. = quinine hypodermatic injections.

1. *The Mild Form, Typhus Levissimus.*—The symptoms are those of the typical disease modified as respects intensity, and in particular as to the febrile movement, which is of lower intensity. The commencement of the attack is usually gradual. There are prodromes; chilly sensations occur; there are headache, diarrhœa, epistaxis, and a scanty or well-marked eruption of rose spots. On the fourth or fifth day the temperature reaches 103° F., but rarely exceeds that level. The defervescence is by lysis, and may occur at the end of the second or during the course of the third week.

2. *The Latent or Ambulatory Form, Walking Typhoid.*—All the symptoms are mild. There is general malaise, prostration, and elevation of temperature, slight diarrhœa. The patient is about, attends to his work, and does not regard himself as sufficiently ill to go to bed. The attack

extends over three or four weeks, and the intestinal lesions proceed to sloughing and ulceration. Herein lies the danger of this form of the disease. Hemorrhage or symptoms of perforation may at length reveal the true nature of the attack, or sudden maniacal delirium may occur.

FIG. 18.

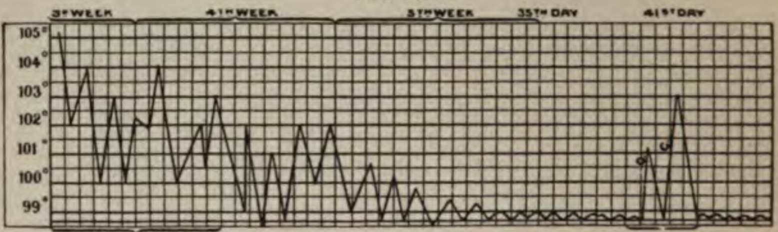


Cold tub-baths.

Abundant malarial organisms.

Dr. W. Gilman Thompson's second case of malarial fever associated with enteric fever.

FIG. 19.



Cold tub-baths.

C. C. = chills.

Pigment found in blood-corpuscles, but no germs.

Same as Figure 18. Third case.

3. *The Abortive Form.*—Prodromes are of short duration or absent altogether. The attack begins abruptly with rigors or a chill. The temperature rapidly attains its maximum. By the evening of the third or fourth day it may reach 104° or 105° F. Rose spots appear as early as the second or third day. At the end of the first or early in the second week defervescence takes place by lysis, often being completed in from twenty-four to seventy-two hours, the fall of temperature being accompanied by profuse sweating. Convalescence is rapid, but relapses may occur. This form of enteric fever appears to be not uncommon in Europe. In this country it is certainly rare.

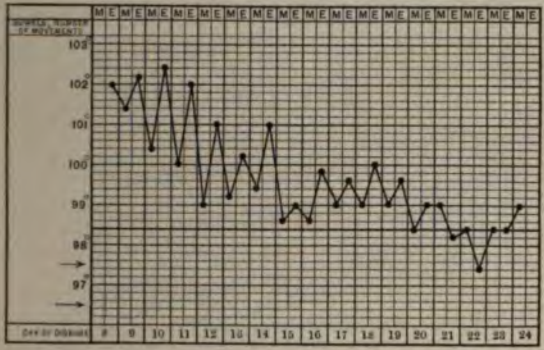
4. *Hemorrhagic typhoid*—a very rare form, commonly fatal, characterized by hemorrhages into the skin and from mucous surfaces. This form corresponds to the hemorrhagic forms of variola, measles, and other infectious diseases, and is not to be confounded with ordinary cases of enteric fever in which hemorrhage from the bowels occurs.

5. *Afebrile Typhoid Fever.*—Dr. Cayley states that many cases and even epidemics of typhoid have been met with in which the temperature has been normal or subnormal throughout the whole course of the disease. He cites an epidemic observed by Strube at the siege of Paris. The symptoms are those of ordinary enteric fever. The duration of the attack was short. Of 23 fatal cases, death took place in 20 during the

course of the first fourteen days. The abdominal symptoms were slight, but the lesions were found upon post-mortem examination.

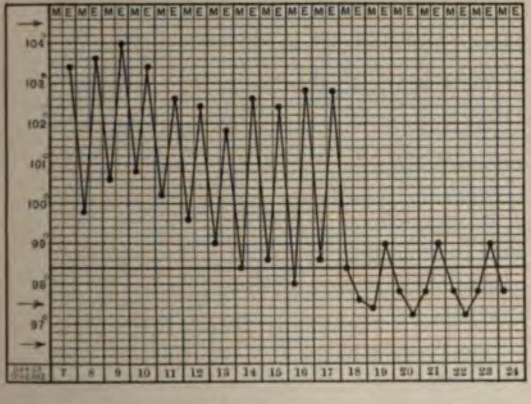
6. Infantile Remittent Fever.—This term has been applied to enteric fever as it occurs in children, for the reason that the pyrexia often assumes a distinctly remittent type throughout the whole course of the ttack. The disease is rare in the first year of life, but not infrequent during later infancy and childhood. The symptoms and complications are modified by the age of the patient. Nose-bleeding is not common; the rise of temperature to the fastigium is abrupt; nervous symptoms are prominent; diarrhœa is uncommon. Other abdominal symptoms are, as a rule, less prominent than at later periods of life. On the whole, the reaction to the infection is less marked. Nevertheless, grave cases occur. Exceptionally, fatal hemorrhage and perforation have been noted. Fatal intestinal hemorrhage occurred in a child twenty-two months old, in which, upon post-mortem examination, the characteristic lesions of

Fig. 20.



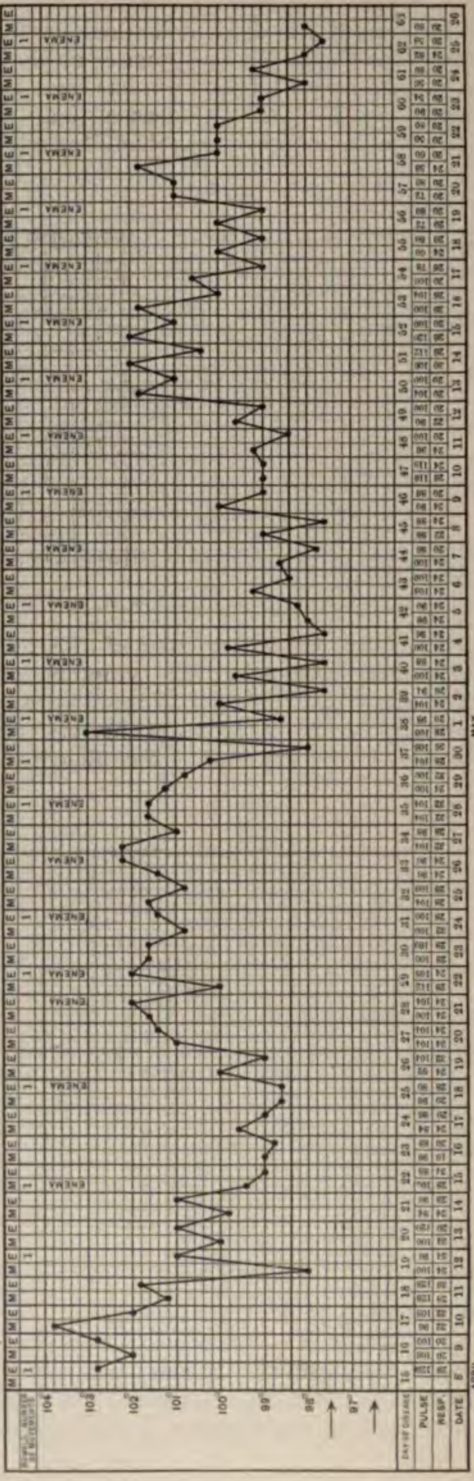
Enteric fever in child aged nine years.

Fig. 21.



Enteric fever in child aged four years, remittent type.

FIG. 22.



Enteric fever, double relapse (Pennsylvania Hospital).

enteric fever were found. Henoch has reported a case in which hemorrhage occurred in a girl ten years old in the course of a relapse which took place in the third week. There was at first an insignificant bleeding, which was followed upon the next day by a very copious hemorrhage with fatal collapse.

Henoch observed perforation in a boy aged eleven in the fifth week after convalescence had been apparently established. Statistics present a wide range of variation in regard to the frequency of perforation in children. Among 232 cases, according to Barthez and Rilliet, it occurred in 3 only; among 73 persons in whom this accident was noted, Murchison found 14 to be under fifteen years of age.

Certain sequels appear more frequently in children than in adults. Among these are noma, lesions of the bones, and aphasia. The death-rate in children in the first year is high, especially among the new-born. The mortality in childhood after the first year is decidedly lower than in adults.

7. *Enteric Fever in the Aged.*—In the advanced periods of life enteric fever runs a modified course. Its onset is insidious; the febrile movement is less intense, and during convalescence the temperature falls to markedly subnormal ranges. The eruption is frequently absent and diarrhœa is less common. Perforation rarely occurs. Murchison encountered it twice in patients over forty years of age, and I saw it in the body of a man aged fifty-three. Complications are frequent and grave. Broncho-pneumonia and croupous pneumonia occur, and there is especial danger of collapse from cardiac asthenia. The mortality of enteric fever after the fortieth year of life is high.

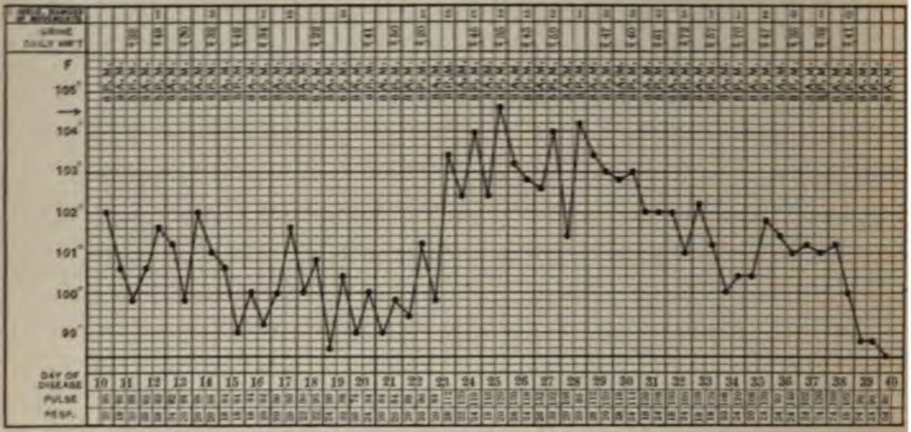
8. *Enteric Fever in Pregnancy.*—Pregnant women seem to enjoy a relative immunity. This immunity would appear to be greater during the last than during the first half of the pregnancy. Of women who in this condition contract enteric fever, more than 50 per cent. abort, this accident occurring usually in the second week of the attack. The fœtus has been found to be infected, and successful cultures of the bacillus of Eberth have been made from the viscera.

RELAPSE.—The relapse of enteric fever is the manifestation of reinfection. It is attended by a repetition, with some modifications, of the fever and associated phenomena, a new eruption of rose spots, fresh glandular infiltration, and enlargement of the spleen. The relapse is, as a rule, of more abrupt onset and of shorter duration than the primary attack. It is commonly separated from the latter by an interval of some days, during which the temperature range is subnormal or normal. During this period in cases in which relapse occurs the spleen remains enlarged. The relapse is not invariably separated from the primary attack by an interval of apyrexia, but may develop during its course. It is then termed an intercurrent relapse, and to intercurrent relapse must be ascribed many of the cases of unusual prolongation in the absence of complications. Two or more relapses may occur. As many as five relapses have been reported (DaCosta). I have observed four well characterized relapses in a young adult.

The frequency of relapse is variable. It ranges from 3 per cent. (Murchison) to 15 or 18 per cent. (Immerman). In 284 cases under fifteen years of age observed in the Boston City Hospital from 1882 to

1895 and analyzed by Morse relapse occurred in 11 per cent. A large proportion of the cases of enteric fever in infancy and childhood are of mild intensity. The statistics of hospital and private practice with reference to this disease in the earlier periods of life are at variance. In private practice relapse appears to be much less common in childhood than in adult life. This discrepancy is to some extent due to difference of opinion among practitioners as to what constitutes a relapse.

Fig. 23.



Intercurrent relapse following mild primary attack (Philadelphia Hospital).

Relapse has been confounded with recrudescences of fever occurring during convalescence. Such rises of temperature are usually brief, not lasting more than a day or two. Occasionally they are of longer duration, and are due to infectious or inflammatory sequels. Under these circumstances careful investigation will usually reveal the nature of the pathological process. Elevation of temperature during convalescence, unattended by rose spots, enlargement of the spleen, intestinal symptoms, and of brief duration on the one hand or protracted duration on the other, should not be regarded as constituting true relapse. The relapse declares itself by a step-like rise in temperature. Sometimes the rise is abrupt and progressive; at others morning remissions occur, but usually the maximum is attained in the course of from three to five days. The subsequent course of the fever corresponds very closely to a primary attack, except that it is, as a rule, of shorter duration. Of 53 cases noted by Murchison, the mean duration of the primary attack was about twenty-six days, of the interval about eleven, and of the relapse about fifteen days. There is danger of the fatal issue from the stress of the disease when the attack is protracted by relapse or repeated relapses, but death may occur in consequence of any of the events which bring it about in primary attacks. Post-mortem examination of the bodies of those who have died in relapse of enteric fever has revealed the lesions of the primary disease. The individual intestinal lesions are less numerous, for the reason that only those glands and patches of Peyer are involved that escaped during the first attack. The ulceration is therefore higher up in the ileum and coexists with the recent cicatrices of the primary attack, which are most numerous and extensive just above the ileo-cæcal valve. Relapse is due to reinfection from within the body of the patient. It is, in fact, a repetition of the primary attack. To the question why the primary attack confers immunity in a majority of instances, fails to confer a lasting immunity in a few, and renders the patient liable to prompt reinfection in from 3 to 15 per cent., no satisfactory reply has yet been made.

Second Attacks.—The attack of enteric fever in a great majority of instances confers complete immunity against subsequent attacks. To this rule there are, however, exceptions. Many cases have been recorded in which a second or even a third well authenticated attack of enteric fever has occurred in consequence of remote independent infection in the same individual. I have personal knowledge of a case in which the patient suffered from three attacks of enteric fever at intervals of some years, the third proving fatal. To the immunity acquired in infancy and childhood must be attributed the insusceptibility of many adults upon exposure.

DIAGNOSIS.—Well developed cases of enteric fever after the first week may be usually recognized without difficulty. During the first week it is, however, often impossible to form a positive diagnosis, but even then the nature of the disease may be suspected if there be febrile movement with nocturnal exacerbations, each night attaining a higher temperature, and especially if there be headache, epistaxis, diarrhœa, either spontaneous or readily produced by laxatives, progressive asthenia, and, toward the end of this period, appreciable enlargement of the spleen. The direct diagnosis of the developed disease finds its support in the continuance of the febrile movement and the appearance of abdominal symptoms—namely, diarrhœa, pain, enlarged spleen, moderate tympany, and lenticular rose spots. In doubtful cases the coincident occurrence of cases in the same house or locality is of diagnostic importance.

The differential diagnosis from certain other acute febrile disorders is sometimes attended with difficulty. The diseases with which enteric fever is liable to be confounded may be divided into two groups—first, those which resemble it in the first week of its course, and, second, those which resemble it in its more advanced stages. To the first group belong febricula, influenza, and in children certain of the exanthemata in the pre-eruptive stage. Differences in the mode of onset, the short duration of febricula, the epidemic prevalence of influenza, are facts of importance in diagnosis. The prominence of coryza and bronchial catarrh would suggest the possibility of measles, and erythematous angina would lead us to suspect scarlet fever, while intense headache and the presence of lumbar pains would serve to distinguish variola from enteric fever.

To the second group belong certain forms of malarial fever, acute miliary tuberculosis, appendicitis, peritonitis, trichinosis, and, in children, entero-colitis.

Malarial fever and enteric fever, as has been demonstrated by W. Gilman Thompson,[1] may coexist in the same patient. This association is unquestionably rare, and cannot be regarded as establishing the existence of such a nosological entity as typho-malarial fever. Some forms of malarial fever closely resemble enteric fever, especially when the marked abdominal symptoms are present. Vomiting, diarrhœa, splenic enlargement, cerebral symptoms, and the condition known as the typhoid state may occur in both diseases. The more important points of distinction are to be sought in the presence of the eruption and the discovery of malarial bodies upon examination of the blood. The absence of the characteristic rash of enteric fever is without positive diagnostic value in doubtful cases, since in a small proportion of the cases the eruption does not show itself during the whole course of the attack.

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[1] *Trans. Assoc. Amer. Phys.*, 1894.

Acute tuberculosis presents in some instances a close resemblance to enteric fever. In the latter disease, however, the temperature in a majority of instances conforms more or less closely to a definite type, whereas that of tuberculosis is extremely irregular. In enteric fever diarrhœa and tympany are common; in tuberculosis, diarrhœa when present is of a different character and the abdomen is flat, often scaphoid. In enteric fever nose-bleeding and enlargement of the spleen occur; in tuberculous processes these symptoms are rare or absent altogether. The headache of enteric fever is usually dull; that of tuberculous meningitis is acute and frequently associated with intolerance of light and sound. In enteric fever vomiting is much less common than in tuberculous meningitis. Convulsions are likewise rare in enteric fever, and the headache usually disappears upon the occurrence of delirium, whereas in tuberculous meningitis headache and delirium may alternate from the beginning. In this connection it is important to emphasize the fact that in rare cases of the so-called cerebro-spinal form of enteric fever the onset of the attack is abrupt, with intense headache, photophobia, painful retraction of the muscles of the back of the neck, twitching, delirium, and vomiting. Under these circumstances the diagnosis of enteric fever cannot be made until about the end of the first week, when the appearance of abdominal symptoms and rose spots, very often coincidently with subsidence of the cerebro-spinal symptoms, declares the true nature of the infective process.

Croupous pneumonia may also occur early in the course of the attack, or pulmonary localization may cause enteric fever to simulate pneumonia. In certain cases it is not possible to determine whether the pulmonary phenomena are the results of an intercurrent process or of an early localization of the enteric fever infection.

Appendicitis in rare instances may simulate enteric fever. The course of the temperature, the absence of splenic enlargement, the localization of the abdominal phenomena in the right iliac region are of diagnostic importance.

Peritonitis due to other causes than perforation is to be discriminated from that occurring in the course of enteric fever, by the antecedent history of the case. If the patient, however, does not come under observation until after the appearance of the symptoms, it may be impossible to determine whether they are due to perforation or not. The presence of the rose spots would be of importance in the decision of this question.

Trichinosis is attended with pyrexia, vomiting, and diarrhœa. Epistaxis and splenic enlargement are rare; rose spots do not occur. On the other hand, the symptoms of the myositis and the local and general œdema, so frequent in trichinosis, are absent in enteric fever.

Entero-colitis may in children be confounded with enteric fever. The fever and constitutional disturbances are symptomatic of the local trouble. The spleen is not commonly enlarged, abdominal pain is conspicuous and severe, and rose spots are absent.

PROGNOSIS.—The death-rate is much influenced by treatment. It ranges under ordinary conditions from about 7 per cent. under systematic cold bathing to about 15 per cent. under expectant symptomatic treatment. Murchison found in 27,051 cases collected from various sources a death-rate of 17.45 per cent.; Jaccoud, in a collection of 80,140 cases treated on the expectant plan, a mortality of 19.23 per cent.; 17,000 cases in Vienna showed a mortality of 22.5 per cent. According to Cayley, the principal Continental hospitals have a mortality varying between 16 and 25 per cent. Some years ago Delafield collected from the records of the New York hospitals, extending over a period of about five years, 1305 cases, with a mortality, estimated by years, varying between a minimum of 20.1 per cent. in 1879 and a maximum of 30 per cent. in 1880. The available statistics of recent years unquestionably show a reduction under various plans of treatment.

The mortality in childhood, taking all the cases together, is decidedly lower than in adults. Enteric fever, like all the acute infectious diseases, shows an extremely variable intensity in children, the severe cases, however, being the exception rather than the rule.

The prognosis in individual cases must be guarded, since it not infrequently happens that in cases running an apparently favorable course death occurs toward the end of the third or during the fourth week from some unforeseen accident or complication. The prognosis is unfavorable in cases in which the intensity of the infection is manifested by the rapid development of severe symptoms—intense pyrexia, cardiac asthenia, ataxic phenomena, and the occurrence of multiple cases in the same house or in the immediate locality; it becomes unfavorable likewise upon the development of intestinal symptoms of high grade, such as copious diarrhœa, abdominal pain, or meteorism. Recurrent vomiting has also an unfavorable prognostic import. Finally, intestinal hemorrhage, perforation, and such complications as ulcerative endocarditis, meningitis, diphtheria, large pleural effusions, and in children the exanthemata arising as intercurrent or consecutive affections, render the prognosis extremely grave.

Sudden death may occur about the time of defervescence or in early convalescence in consequence of extreme cardiac asthenia.

Corpulent persons bear enteric fever badly. Those whose habits have been intemperate and those who suffer from disease of the kidney and the gouty are especially liable to the gravest accidents of the disease. The death-rate is slightly greater in women than in men.

TREATMENT.—(*a*) **Prophylaxis.**—Enteric fever is theoretically a preventable disease. The objects of prophylaxis are (1) to prevent any case of the disease from becoming a focus of infection, and (2) to correct such faulty sanitary arrangements as lead to the pollution by fecal matter of water used for drinking and domestic purposes. The successful pursuit of these objects wherever the disease prevails would certainly be followed immediately by a notable decrease in the morbidity. Rational preventive measures, even though imperfectly carried into effect, have been followed by remarkable results. Their general adoption and rigid execution would be followed by a very great reduction in the prevalence of the disease.

The first measure of prophylaxis—namely, the prevention of the spread of the disease from any patient as a focus of infection—constitutes an important duty of the physician in attendance. The typhoid bacilli in the fecal discharges can be at once and absolutely destroyed upon the spot. They do not appear in the stools until some time after the period at which under ordinary circumstances the patient comes under the care of the physician. It follows from the facts now established in regard to the transmission of the disease that any given case may be prevented from becoming not only a source of infection to those in his immediate vicinity, but also to those at a distance. Upon those in immediate attendance devolves the duty of protecting alike persons in the vicinity of the patient and those to whom the disease may be conveyed by the contamination of running streams or other sources of water supply or in cities by way of sewer systems transmitting the infecting principle.

To this end the fecal discharges of every case and the urine should be at once and effectually disinfected. For this purpose a solution of chlorinated lime of the best quality, containing at least 25 per cent. of available chlorine, of the strength of 6 ounces (192.) to the gallon (4 litres), may be employed. Commercial sulphuric or hydrochloric acid and water in equal parts will disinfect a stool in two hours. A solution of mercuric chloride, 1 : 500, acidulated with tartaric or hydrochloric acid, will disinfect an enteric fever stool in six hours. Carbolic acid in 5 per cent. solution is less efficient and requires twenty-four hours. Milk of lime, prepared by slaking freshly burned quicklime and stirring up the powder with twice its volume of water, is an efficient and rapid disinfectant for enteric fever stools. This preparation should be freshly made and added to the stool in equal bulk. When the bed-pan is to be used, it should contain one half pint (250 c.c.) of the solution employed. Directly after the movement of the bowels a pint (500 c.c.), or as much as a quart (1000 c.c.), of the solution, according to the amount of the dejection, should be poured over it. The contents of the pan should then be thoroughly mixed by agitation of the vessel, and solid masses should be broken up with a glass rod, which can be thoroughly disinfected. If a stick is used, it should be forthwith burned. The pan should then stand two or three hours before it is emptied into the water closet or privy vault. The nurse should be made to understand that prolonged exposure is necessary to complete disinfection.

Clear solutions like that of the mercuric chloride should be colored by the addition of potassium permanganate, and the disinfectants employed must be kept in a place by themselves and conspicuously labelled "Poison." Commercial preparations placed upon the market under various names for the purpose of household and sick-room disinfection are not to be prescribed. They are of unknown and doubtless inconstant composition, and unduly expensive. When acid disinfectants are employed the water closet is to be flushed for some minutes several times during the day to diminish their action upon the fittings and connections. In country places the thoroughly disinfected stools may be emptied into an ordinary privy without risk, or they may be mixed with fresh earth and buried in a trench at a distance from all sources of water supply. It is imperative that they be thoroughly disinfected. In some localities it is the custom to dispose of enteric fever stools by mixing them with sawdust and burning them. Privy vaults that are to be disinfected may be treated by slowly pouring into them a solution of mercuric chloride (1.5–1 kg. in several gallons of water), or by freely scattering over the contents of the well quick-lime or chlorinated lime from day to day.

The danger of the spreading of the infection by way of the accidental soiling of the patient's clothing or bed-clothing with the fecal discharges is not to be disregarded. It is important that the mattress of an enteric fever patient should be covered by a rubber sheet, and that articles of bedding and the patient's clothing should, when accidentally soiled, be immediately removed. Should fecal discharges have become dried upon these articles, the stain should be moistened with a disinfectant solution before removal. There should be in the sick-room a tub into which the garments of the patient, his bed-linen and towels, should be immediately placed and moistened with a 5 per cent. solution of carbolic acid before removal to the laundry, where they must without handling be at once boiled for half an hour. They should then be washed with soft soap and thoroughly rinsed. After drying they must be aired and exposed to the sun for several hours before being again used. In fatal cases the corpse must be enveloped in a sheet wet with a carbolic acid solution, 1 : 20. After the recovery of the patient the bedstead and furniture of his room are to be washed with a solution of mercuric chloride, 1 : 1000. Bedding, towels, and the like are to be thoroughly boiled. The rubber coverings are to be first disinfected and then destroyed. In a private house the room should be aired daily for a fortnight before it is again occupied.

At the time of an epidemic of enteric fever all drinking water and milk used in families should be subjected to boiling for thirty minutes. New comers and temporary sojourners in a locality in which enteric fever is prevalent should drink only boiled water and milk and should avoid the use of uncooked vegetables. In sporadic cases search should be made for the source of the infection. In the great centres of population such investigations, except in so far as they indicate general defects in the water supply or in the sewage, are not attended with satisfactory results, but when enteric fever occurs in the form of an epidemic, limited to a locality supplied with water from a particular source or to a neighborhood served with milk from the same dairy, the results are often in the highest degree significant. They show defects in the water supply or milk contamination, and point to the circumstances under which pollution has taken place, and even indicate with precision the measures by which further infection is to be prevented. The results of such investigations are especially valuable in restricted localities into which the cause of the disease has been conveyed by the advent of cases of enteric fever.

The second object of prophylaxis—namely, the correction of faulty sanitary arrangements by which the pollution of water used for drinking and domestic purposes by fecal matter or the infection of milk and other articles of diet by such water is rendered possible—falls clearly within the scope of the health organizations of local governments. The inadequate powers vested in State and local boards of health, the ignorance of officials, and, above all, the apathy of the people, conspire to render hope of the attainment of this object, even in enlightened communities, remote. No outlay, however, will prove more profitable for the taxpayer. The actual money cost of a polluted water supply and bad drainage as factors in the production of disease cannot be computed. It is certain, however, that the value of the lost time, cost of support, nursing, and the like would amount in a large city to much more than sufficient to rectify the unsanitary conditions to which endemic enteric fever is directly due.

An abundant and good water supply is of first importance. The natural history of the water is better evidence of its purity than the response in occasional samples to chemical and biological tests. The most desirable sources of supply are to be found in mountain lakes or streams in unpopulated districts or in artesian wells. The impossibility of protecting streams that flow through populous valleys or in preventing the contamination of ordinary wells is obvious. It constitutes, therefore, an essential measure of prophylaxis in cities and towns to abandon wells, and those communities which derive their water supply from streams receiving the sewage of other towns and villages can escape the endemic and occasionally epidemic prevalence of enteric fever only by filtration upon a large scale and in accordance with scientific methods before distribution.

Mosny showed that the death-rate from enteric fever in Vienna diminished from 11.5 per 10,000 to 1.1 per 10,000 after the introduction of water from the neighboring mountains. When, however, a few years later, owing to a defect in the waterworks, it became necessary to again use the water of the Danube for a short period, an epidemic broke out which was confined to those parts of the city to which this water was distributed. Similar results followed the use of the water of the Seine for drinking purposes in Paris.

A supply of good water is not in itself, however, sufficient to reduce the endemic prevalence of enteric fever to the lowest point. A correspondence between the morbidity from this disease and the drainage exists which has not yet been fully explained. This correspondence has been especially demonstrated by the observations of E. F. Smith and Osler. The introduction of thorough drainage systems constitutes a means of general prophylaxis against enteric fever second in importance only to that of a poor water supply. Such drainage systems, however, discharge usually into running streams, and therefore transfer the danger to other localities more or less remote. Thus outbreaks of enteric fever have occurred in the crews of ships lying at anchor near the sewer outlets of large cities in consequence of using water for drinking purposes. Exact facts as to the distance to which typhoid bacilli may be transported, and the length of time during which they retain their virulence under these circumstances in large bodies of water, have not yet been definitely fixed. The occurrence of local epidemics of enteric fever in consequence of the consumption of oysters taken from waters polluted by the sewage of cities is most important. It is therefore obvious that the immediate and efficient disinfection of all the stools in every case of enteric fever in the sick-room is an imperative measure of prophylaxis.

(*b*) **The General Management of the Patient.**—The result of the treatment in enteric fever is largely influenced by the details given to the general management and nursing of the case. The patient should not be exposed to continued infection. Obvious faults connected with the water supply or milk supply should be immediately corrected. Under these circumstances it is necessary to remove the patient to more favorable surroundings. In hospitals enteric fever patients have usually been treated in the ward side by side with other patients. This practice is without danger if precautionary measures are taken to secure the immediate disinfection and removal of the dejections and the cleanliness of the patient's person and bedding. It is, however, at present considered better to place enteric fever patients together in separate wards. In general practice patients, as a rule, come under observation during the period of prodromes or early in the first stage of the disease. If the symptoms are such as to give rise to a suspicion that the disease is enteric fever, the patient should be ordered at once to bed. In the event of the malady not being enteric fever, the patient's interests do not suffer. If, however, the symptoms be those of developing enteric fever, rest in bed will favorably influence the later progress of the attack. The general course of cases treated from the beginning of the attack is more favorable than that of those coming under medical care after the disease has made some progress. Persons who struggle against the early symptoms of the attack, or who continue to go about until the intensity of the febrile movement, diarrhœa, or sheer prostration obliges them to betake themselves to bed, constitute the worst cases of the disease. The fatigue of long journeys undertaken to reach home after the development of the symptoms has frequently exerted an unfavorable influence upon the subsequent course of the attack. Rest in bed from the beginning of the sickness is important. Patients treated upon the expectant or expectant-symptomatic plan should not be allowed to rise until some days after defervescence has been completed.

The urinal and bed-pan must be regularly used. Many patients who declare that it is impossible to empty the bowel in the recumbent posture find upon trial that it is less difficult than they supposed. Strict rules in regard to rest in bed and the employment of the bed-pan and urinal cannot always be carried out in the case of young children.

The room should be large, well ventilated, and, if practicable, have a southern exposure. All curtains, hangings, and pictures should be at once removed. Only such simple furniture as is necessary for the attendants should be retained. An open fireplace is advantageous. Free ventilation is necessary. Drafts are to be avoided, but the fever patient is with ordinary care little liable to take cold. In grave cases the patient may be with advantage removed at intervals from one to the other of communicating rooms. In cities a back room removed from street noises is desirable. When the weather permits the patient may with advantage be removed during the day for a few hours to a porch or gallery in the open air and sunshine. A narrow single bed, not too high, greatly lightens the labor of nursing. The mattress must be smooth, firm, and elastic. A rubber cloth or mackintosh must be placed under the sheet. The covering should be light and varied from time to time according to the sensations of the patient. Bedding or bed-clothing soiled by the involuntary evacuation of urine or fæces should be immediately changed and disinfected. In very severe cases it is desirable to use two beds, placed side by side, from one to the other of which the patient when necessary may be lifted.

The wants of the patient are to be attended to quietly, noiselessly, without conversation or comment. During convalescence the visits of friends are to be restricted in number and should be very brief. At this period tact and caution in the communication of details of business affairs and matters of annoyance are most important.

Patients who have been delirious must under no circumstances, though at the moment apparently rational, be left alone until convalescence has been fully established. Suicidal impulses may develop, and many patients have destroyed themselves during the momentary absence of the attendant. Good nursing is of the highest importance. It means to the physician accurate and systematic information at his visits, alertness and responsibility in his absence. To the patient it means quietude, gentleness, neatness, diminished suffering. To both the physician and patient it means the best use of the resources of medicine.

The free administration of fluid is necessary. Many patients, apparently fully conscious, fail to obtain the necessary amount of drink. Fluid, therefore, should be offered in small amounts at short intervals. A judicious nurse, administering fluid in small amounts at a time, is not likely to give in the aggregate too much.

Pure cold water is the best drink for fever patients. The aërated mineral waters afford an agreeable change.

The *diet* throughout the attack should be nutritious, easy of digestion, and liquid. Definite and explicit directions as to kind, quantity, and the intervals of administration are necessary. The details must be systematically recorded. General directions on the part of the physician and general reports on the part of the nurse are inadmissible. The amount is to be regulated by the requirements of individual cases. Indigestion and an aggravation of the symptoms of intestinal catarrh result from over-feeding. On the other hand, under-feeding increases the asthenia and prolongs convalescence. As a rule, the mental condition is such that the patient takes without objection whatever is proffered in the way of food or medicine. Enteric fever patients are usually rather over-fed than under-fed. The signs of gastric indigestion, increased diarrhœa, and the presence of milk curds in the stools will call the attention of the physician to the fact that the patient is receiving too great an amount of food. Despite theoretical considerations, milk holds the first place among fever foods. It supplies the liquid required for the chemical processes of nutrition; it is in most cases readily digestible; it is diuretic; it may in a majority of the cases constitute the sole diet or at all events the basis of the diet. Used alone, milk should not much exceed in daily amount for an adult 3 pints (1500 c.c.) during the first period of the disease, or 2 quarts

(2 litres) subsequently. This quantity must be given in divided portions at intervals during the twenty-four hours. Milk as a fever food may be raw or boiled, warm, cold, or iced, or now and then given coagulated into soft curds by means of rennet. It may be diluted with lime-water in the proportion of 1 part to 5, or mingled with one-third its volume of Vichy water. The repugnance evinced by some patients to a milk diet may be overcome in part by the addition of coffee or spirit, such as brandy, whiskey, or rum; the inability of others to digest it may be overcome by partial peptonization or by its administration in the form of koumyss, kefir, or matzoon. Sterilized milk may be used for a time with advantage, but its continuous employment cannot be recommended. The occasional administration of buttermilk or wine whey may vary an otherwise monotonous diet. A raw egg beaten up in the milk, with or without spirit, reinforces the diet, and in the German Hospital we frequently administer three or four raw eggs during the course of the twenty-four hours to cases under the bath treatment. If there be irritability of the stomach, the white only of the egg, mixed with an equal volume of water and flavored with a little brandy or sherry, is better borne. It is usually desirable to vary the diet, and in some cases it is impossible to administer milk continuously. We may then employ broths or soups prepared from beef, mutton, chicken, or veal flavored with vegetable juices and containing a little rice or barley. These should be, however, systematically strained. Consommé, either hot or frozen according to the fancy of the patient, clam-juice, oyster soup, thin barley gruel, arrowroot, and the commercial malt foods, peptonoids, and the freshly expressed juice of partly broiled beef, may be included in the dietary. A cup of hot coffee or cocoa, well diluted with milk, may be given once in the twenty-four hours, preferably in the early part of the day. Food should be systematically administered every two or three hours during the day and at intervals of three or four hours at night. In grave cases, where the amount taken at a time is small or the prostration is extreme, these intervals must be shortened. A restless patient who has just fallen into a quiet sleep must not be disturbed for food. Patients who are very somnolent or soporous must, if possible, be roused before food is given, in order to diminish the danger of inhalation pneumonia.

Solid food is not to be administered until the evening temperature has been normal for a week. The change even then must be tentative and gradual by way of milk toast, custards, light puddings, and similar articles of diet to the ordinary every-day food. The details of the diet in young children must be regulated in accordance with the age of the patient and the previous plan of feeding, no radical departure from the usual nourishment being necessary beyond the avoidance of every kind of solid food.

Alcoholic stimulants constitute an essential element of the routine procedure in the treatment of enteric fever by systematic cold bathing, and their administration will be discussed in connection with that plan. In other forms of treatment the circumstances under which alcohol is to be administered demand careful consideration. Those who recall the method of its employment some years ago agree that it was very often given as a matter of course when not required, and nearly always in un-necessarily large amounts. At the present time alcohol is frequently used too freely in the sick-room. In mild cases of enteric fever and in young persons of previously good health and habits it is, as a rule, not required. In persons of feeble constitution and those past middle life, and in all severe cases, alcohol should be systematically but cautiously administered. To those who have previously been accustomed to its use it should be given from the onset of the attack, and to a guarded extent in amounts suggested by the habits of the patient. It is important that alcoholic stimulants should be given in guarded amounts during the early period of the attack prior to the subsidence of the headache—an event that commonly occurs between the end of the first and the middle of the second week. After this time alcohol may be used more freely.

Alcohol is clearly indicated in all cases in which there is great general prostration. Its administration is essential where there is weakness of the heart's action, as shown by a small, feeble, and irregular pulse, a feeble cardiac impulse, and a faint first sound. It should be administered with a free hand upon the development of delirium, tremor, or other ataxic symptoms. Its use is especially important when diarrhœa, tympanites, and great tenderness indicate extensive and deep ulceration. The administration of alcohol is imperatively demanded in all severe cases and upon the development of serious complications, such as bronchitis of the smaller tubes, broncho-pneumonia, croupous pneumonia, pleurisy, or peritonitis. The amount must be regulated according to its influence upon the symptoms for which it has been prescribed in individual cases. The character of the first sound of the heart and the pulse and the nervous symptoms constitute the best guide for the dose and the frequency of its administration. If the urine be albuminous, and particularly if it contain casts, alcohol is to be given cautiously, and its effect upon the amount and character of the renal excretion is to be studied from day to day.

Under ordinary circumstances the administration of alcohol should begin with small quantities, to be increased according to the requirements of particular cases. Four to eight ounces (125–250 c.c.) of spirit or from a pint to a pint and a half (500–750 c.c.) of claret, burgundy, or champagne in the course of twenty-four hours yield the best results. In serious cases much larger quantities may be required. Whiskey or brandy may be given with milk in the form of punch, or, if the patient prefer it, diluted with water. Where small amounts of alcohol are indicated wine whey constitutes an agreeable means for its administration.

(*c*) **The Special Management of Individual Cases.**—The milder cases do well without drugs. Rest in bed, skilled nursing, and a carefully regulated dietary comprise all that is necessary in the management of the case. With moderate fever, a good heart, no signs of serious intestinal lesions, and the absence of pulmonary complications beyond a slight bronchitis, the administration of medicines is needless. The treatment may with advantage be commenced with laxative doses of castor oil or of calomel, which should be repeated at intervals of three or four days until the middle of the second week of the attack. Later than this constipation may be relieved by enemata of lukewarm water in which is dissolved common salt in the proportion of a teaspoonful to the pint, or by soapsuds or by thin gruel. In the event of constipation not being thus relieved, enemata of glycerin and water or glycerin suppositories may be employed. These measures to secure the action of the lower bowel do not require repetition at intervals shorter than every third day. There are those who upon theoretical grounds regard the systematic washing out of the lower bowel by large enemata of normal salt solution once or twice in the course of twenty-four hours as of advantage.

Cases treated with so-called fever mixtures or with small doses of quinine, the mineral acids, turpentine, silver nitrate, or other drugs that have no effect upon the course of the disease must be regarded as managed in accordance with the expectant method. Fortunately, such medicaments are usually well tolerated by the patient. The great variation in the intensity of the attack in different cases must put us on our guard against ascribing to therapeutic measures results that are really to be attributed to the course of the disease in individual cases.

(*d*) **Treatment of Special Symptoms and Complications.**—The *headache* of the period of onset requires, as a rule, but little treatment; it disappears spontaneously between the end of the first and the middle of the second week. Quietude, the exclusion of light, compresses to the head wet with cold or hot water according to the sensations of the patients, are very often sufficient to control the headache. . Applications of Cologne water, of spirit of camphor, of menthol, or of chloroform are sometimes acceptable. If headache, however, persists, or is, despite the foregoing measures, distressing, antipyrine, acetanilid, or phenacetin given in small doses repeated at short intervals are efficacious. Drugs of this class are, however, to be used in enteric fever with caution.

Sleeplessness may become a troublesome symptom in the early course of enteric fever. It very often diminishes during the course of the second week. It may, however, be persistent and exhausting. The insomnia of the early course of the attack may be usually readily controlled by appropriate doses of sodium bromide or chloral, used either separately or in combination. Sulphonal, trional, urethan, and chloralamide are hypnotics of inferior value. Opium and its derivatives must be regarded as objectionable in the early stage of the disease by reason of their unfavorable influence upon the digestion and the secretions, and their liability to be followed by disagreeable after-effects, such as nausea, vertigo, and the intensification of headache. Later in the course of the disease opium becomes at once the most efficient and safest means of controlling insomnia and excitability, its effect upon the secretions being less unfavorable than early in the attack, while its disagreeable after-effects are less marked.

Somnolence, stupor, and delirium must be treated by stimulants and external antipyretics. Among stimulants alcohol takes the first place and stands almost alone; the spirit of chloroform and camphor prove, however, useful in emergencies. The latter may be administered hypodermically in 5 per cent. solution in ether, 10 minims (0.6), being repeated once or twice at intervals of several hours. Ether alone in 10-minim doses, given hypodermically, is of advantage. Ammonium carbonate and the aromatic spirit of ammonia are of inferior value. They are, however, frequently employed in the treatment of pulmonary complications. Pure Siberian musk is a powerful stimulant in conditions of nervous depression. Administered in pill or suppository in single doses of from 5 to 10 grains (0.32–0.65), it sometimes produces decided effects. The difficulty of obtaining it, its great cost, and the uncertainty of its effects preclude its general employment. Hyoscine hydrobromate, codeine, and asafœtida are also useful in the treatment of active delirium, while delirium suggestive of hysteria is often favorably influenced by full doses of valerian, alone or in combination with the bromides.

Such external antipyretics as the ice-cap or the cold douche are indicated where delirium is marked and persistent or there is stupor tending to coma. Applications of cold must be transient and not too frequently repeated, lest they be followed by depression and collapse. It is a good practice to accompany them by warm applications to the feet and legs and sinapisms to the præcordium and epigastrium. The tepid or warm bath or the warm bath gradually lowered exerts a favorable influence upon this group of nervous symptoms. The delirium of enteric fever is, as a rule, manageable. Physical restraint is rarely required, though it occasionally happens, especially in hospitals where the nurses have a number of cases to look after, that it is necessary to confine the patient by a sheet passed over the lower part of his chest and fastened under the bed.

Good nursing is indispensable. The enteric fever patient who has become delirious should never for an instant be left alone.

Tremor, out of proportion to the other signs of nervous prostration, has been regarded by Sir William Jenner as a sign of deep ulceration of the intestine. In any case supervention of tremor is to be regarded as an indication for the administration of alcohol in full doses. Other nervous symptoms occurring during enteric fever do not call for special treatment. Those that persist after the subsidence of the febrile movement are to be treated in accordance with general rules.

Dryness of the tongue and the accumulation of sordes upon the teeth and gums demand the frequent administration of water in small amounts, washing of the mouth with pure water or water containing borax, claret, or small amounts of tincture of myrrh, or the use of a cotton mop wet with a saturated solution of boric acid.

Fissures at the nostrils or at the angle of the mouth or upon the lips may be treated by the occasional application of a soft ointment containing 20 grains (1.3) of boric acid to the ounce (31.).

Vomiting is not a common symptom in enteric fever. Occurring at the onset of the disease, it is usually an indication of profound infection or of extreme gastric irritability. Under these circumstances nourishment by the mouth should be temporarily withheld, while fractional doses of calomel at short intervals or full doses of chemically pure cerium oxalate or of dilute hydrochloric acid or cocaine hydrochlorate, gr. ⅙ (0.01), may be given. At the same time sinapisms may be applied to the epigastrium and iced dry champagne administered in small amounts. In some instances vomiting is due to antecedent lesions of the stomach. When vomiting occurs late in the course of the attack it is very often due to uræmia, and is then associated with other evidences of nephritis.

In all cases the *urine* should be, from the beginning of the attack, systematically examined at intervals of two or three days. A trace of albumin without casts or with a cast here and there—febrile albuminuria—is not in itself of great clinical importance, but a large percentage of albumin with many casts, and especially epithelial or blood casts, indicates the development of an intercurrent acute nephritis.

Constipation late in the course of the attack may be due to the continued use of a diet that is at once concentrated and leaves a minimum of unabsorbed residuum. It may, however, result from torpidity of the large intestine. In the latter case the fecal matter accumulates in the form of scybalæ. This condition may set up a sort of secondary diarrhœa, due to the irritation of the lower bowel and attended with a feeling of tenesmus and local distress promptly relieved by the removal of the cause. Prolonged constipation is not necessarily a sign of mild intestinal lesions. On the contrary, deep ulceration of a single Peyer's patch may arrest peristalsis and thus produce constipation. It is therefore important to avoid the administration of laxative drugs after the middle of the second week. Nor are large enemata, especially if administered with some energy, without danger. Diarrhœa requires no especial treatment so long as the stools are of moderate amount and do not exceed three or four in the course of twenty-four hours. This symptom is frequently due to the use of improper food or excessive amounts of food, particularly milk, the strong animal broths, or beef-tea. The substitution of a suitable diet is followed by relief. In other cases the preparations of bismuth, as the subcarbonate, subnitrate, salicylate, or subgallate, administered by the mouth in full doses, constitute an efficient medication. When necessary small doses of opium may be employed in addition. The so-called intestinal antiseptics, such as naphtalin, thymol, resorcin, and the like, are less useful. The administration of astringents, such as alum, plumbic acetate, silver nitrate, tannic acid, catechu, and kino, in the present state of knowledge lacks the support alike of theoretical basis and empirical result. If the stools be highly fetid or ammoniacal, creasote, salol, or salophen may be given or animal charcoal may be administered in broth.

Tympanites is a very common symptom. When excessive it constitutes an urgent indication for the administration of alcoholic stimulants or for their increase if already employed. Turpentine or camphor in addition to guarded doses of opium must be added to the treatment, and active preparations of pepsin or peptenzyme, alone or together with hydrochloric acid, should be administered with the food. Compresses wrung out of iced water or turpentine stupes should be applied, and very cautious light massage of the abdomen may be useful. Small enemata of iced water and enemata of cold water containing turpentine in emulsion are sometimes followed by good results. The careful introduction of a long intestinal tube will sometimes relieve the distention of the lower bowel. The puncture of the distended gut with a hypodermic needle through the bowel wall is an unwarrantable procedure.

The systematic administration of laxative doses of calomel or castor oil every third or fourth day during the first week or ten days tends to obviate to a great extent excessive intestinal disturbance, whether constipation, diarrhœa, or tympanites.

Intestinal hemorrhage is to be treated by the temporary diminution, or even the complete withdrawal, of food for a time, and by the administration of opium, either by the mouth or by suppository. For the time being even water is to be administered in small amounts. To relieve thirst it is better to permit small pieces of ice to be dissolved in the mouth. The action of the bowels is to be controlled by the further administration of full doses of bismuth. If the loss of blood be excessive, there is imminent danger to life and more active measures are required. An ice-bag should be applied to the abdomen in the region of the right iliac fossa. Opium is to be gradually increased until drowsiness and contraction of the pupils follow. Ergotin may be administered hypodermically at short intervals. Enemata of iced water, not exceeding 4 ounces (120) at a time, may be repeated at short intervals. The astringent preparations of iron either by the mouth or by the rectum, and the employment of gallic acid, turpentine, alum, or lead acetate, are not likely to be followed by direct results. The pillows are to be removed and the foot of the bed elevated upon blocks. Sterilized normal salt solution in amounts of from 4 to 6 ounces (120–180) should in grave cases be introduced by hypodermoclysis at from two to four different points and repeated as required. Fluid restored to the body in this manner is both safer and more effective than intravenous injections. The transfusion of blood is attended with serious risk, and is scarcely to be considered under these circumstances. The fall of temperature and improvement in the mental condition of the patient which follow intestinal hemorrhage are usually transitory; exceptionally, however, they mark the beginning of convalescence. An abrupt fall of temperature of several degrees to the normal or below it, occurring in the mid-course of the attack, will justify the suspicion that hemorrhage has taken place, even though no blood may have yet appeared in the stools. This suspicion will be confirmed by the discovery of local dulness upon percussion in the abdomen, usually tympanitic. After intestinal hemorrhage the diet must for a time be restricted to a minimum, and no effort should be made to move the bowels for a period of at least ten days. Spontaneous evacuations are apt, however, to occur in the course of six or eight days.

Peritonitis calls for the free administration of opium. This drug is to be given in the form of the deodorized tincture in doses of 10 minims (0.62) at intervals of an hour until evidences of its physiological effects show themselves. If opium be not well borne by the stomach, morphia is to be administered hypodermically. No nourishment is to be given except concentrated meat juice, a teaspoonful at a time, together with equal parts of brandy and water in the same amounts. Ice-bags should be applied to the abdomen. Should the patient rally, it is of the utmost importance that the bowels be confined as long as possible. An action will usually occur at the end of several days, even under the continued use of opium. If not, at the end of a week or ten days small lukewarm enemata of water containing glycerin or glycerin suppositories may be cautiously employed. Peritonitis in a small proportion of the cases arises in consequence of infection through the base of an ulcer without perforation; in other instances the sloughing out of the base of an ulcer that causes perforation is preceded by local adhesive peritonitis forming attachments with an adjacent viscus or coil of intestines, thus preventing general peritoneal infection. Under these circumstances in exceptional cases recovery may occur. As a rule, suddenly developing peritonitis is due to perforation of the gut, permitting the intestinal contents to escape into the general cavity of the peritoneum. The occurrence of this accident at the close of defervescence or during convalescence, when appetite is returning, the nutrition improving, and the strength of the patient augmenting, raises the question as to the propriety of cœliotomy in order to suture the lesion, resect the bowel at the point of perforation, establish an anastomosis between uninvolved portions of the intestine, or form an artificial anus, and to carry into effect the proper treatment of the infected peritoneum. In selected cases the hopelessness of ordinary methods of treatment justifies surgical procedure, and this opinion finds support in the fact that a small proportion of favorable results have been reported.

Perforation of the intestine is usually single. Murchison's record showed one perforation in 28, two in 5, and three in 4 cases. R. H. Fitz found in 167 cases of intestinal perforation collected from various sources 138 single perforations and 29 multiple perforations.

During the course of enteric fever palpation of the abdomen is to be practised with great caution by reason of the danger of exciting peritonitis, causing perforations or rupturing the spleen.

Collapse attending intestinal hemorrhage or perforation or sudden heart failure is to be treated by absolute quiet, elevating the foot of the bed, the application of external heat, hypodermic injection of suitable doses of strychnia, atropine, ether, or solutions of camphor in ether.

Epistaxis occurring early in the course of the disease is usually slight, often a mere stain upon the handkerchief, and of diagnostic significance only. Later in the course of the attack it is frequently abundant, but rarely attended with danger. The application of ice to the brow or the instillation of very hot water into the nostril is useful. Persistent epistaxis may render plugging of the nostrils necessary. The administration of ergot, turpentine, and the preparations of iron is frequently employed.

Retention of urine is liable to occur in severe cases. A routine examination of the suprapubic region is important. When necessary the catheter is to be employed: a soft-rubber instrument in the case of the male, a glass catheter in the case of the female, is preferable. The instrument should be thoroughly sterilized; immediately before its introduction the parts about the meatus should be invariably bathed with corrosive sublimate solution, 1 : 2000.

The chest complications of enteric fever are frequently attended with insignificant subjective symptoms. For this reason systematic examination by means of the methods of physical diagnosis is necessary at short intervals.

Dicrotism diminishes, or in some cases wholly ceases, upon the administration of proper doses of alcohol.

Cardiac asthenia demands alcohol and strychnia. Caffeine citrate is also useful. When the failure of the circulation is extreme the pillows are to be removed, the foot of the bed elevated by blocks, and absolute rest in the recumbent posture maintained. Cases of sudden death have occurred as a result of the patient's abruptly assuming the erect posture. In the feeble heart of enteric fever digitalis in small doses is of questionable advantage; in larger doses harmful. The nitrites, and especially amyl nitrite and nitroglycerin, are of service. The hypodermic administration of ether or camphor in ether in 10 per cent. solution is useful. So also is the application of sinapisms or turpentine stupes to the præcordia and epigastrium.

Hypostatic congestion may be to some extent prevented by the systematic employment of measures to maintain the forces of the circulation. The patient's position must from time to time be changed from the dorsal to the lateral decubitus.

Bronchitis when slight requires no special treatment. When severe it must be managed in accordance with general principles. Dry cups, oxygen inhalations, the administration of ammonium carbonate and increased doses of alcohol, are indicated in the graver forms. The dangers of inhalation bronchitis and secondary broncho-pneumonia may be to some extent reduced by thoroughly rousing the patient before the administration of nourishment.

The formation of *bed-sores* may be anticipated, and to a great extent prevented, by proper nursing. Frequent change of posture, the removal of pressure by means of water-bags or air-cushions, scrupulous cleanliness, and attention to the bed must be practised in all cases. Erosions are to be immediately treated upon general surgical principles. The water-bed may become necessary.

The *fever* requires when moderate no special treatment. This is especially the case when the morning remissions are considerable, amounting to 1.5°–2° F. (.8°–1.1° C.). Higher temperatures and slight morning remissions call for the use of external antipyretics. In a fever of so prolonged duration as enteric fever a very high and unbroken temperature must be regarded as a grave symptom, and yet cases marked by such temperatures frequently terminate in recovery. On the other hand, cases in which the temperature at no time rises above 103° F. (39° C.) occasionally prove fatal. The height of the fever is not so much an absolute gauge of the intensity of the infection as it is a manifestation of the reaction on the part of the organism to the toxæmia.

The rapid and extensive depression of temperature following the administration of full doses of antipyrine, acetanilid, phenacetin, and similar pharmaceutical preparations is transient and associated with unfavorable symptoms, such as excessive sweating, cardiac depression, and a tendency to collapse. Furthermore, the effect of these drugs upon the general course of the disease is far from favorable. Their use as antipyretics is to be emphatically discountenanced in the treatment of enteric fever. The same is to be said of the internal and external application of guaiacol. External antipyretic treatment by means of cold sponging, cold compresses, the application of ice, the cold pack, cold or gradually cooled baths, cold affusion, iced-water enemata, and the use of Leiter's coils is equally efficient in reducing temperature and unattended by the hazardous perturbations of the functions of the body that follow the use of the so-called internal antipyretics. Such applications produce an effect in children greater than in adults in proportion as the extent of surface to which the application is made is relatively greater as compared with the volume to be cooled. The effect is more prompt and decided, the disturbances of circulation are greater, and reaction is more tardy. The employment of cold in the treatment of enteric fever in childhood demands, therefore, a degree of caution.

Convalescence is slow. In many cases months elapse before the patient regains his previous bodily and mental vigor. Exceptionally the patient never regains his full strength and powers of endurance. During the week following defervescence the temperature is labile and affected by slight causes. Recrudescences of fever occurring during this period are abrupt and transient. Constipation may cause a slight rise of temperature, which immediately falls upon movement of the bowels. Similar rises of temperature occasionally occur after the first taking of solid food, upon undue exertion, after the visits of friends, or conversations upon matters of business. Patients, therefore, should be assiduously cared for several days after the temperature has reached the normal. During this period temperature observations should be taken in the morning and evening, and the diet should be for at least a week restricted to milk, eggs, custards, light farinaceous foods, animal broths, and jellies. If the case progress favorably, at the end of a week ordinary light diet may be gradually resumed, but the seedy fruits and other hard substances liable to pass through the intestines unchanged are to be avoided. During the early convalescence the craving for food is often such that patients complain bitterly both of the quantity and quality of their sick-room fare. If during convalescence diarrhœa persist, the diet is to be carefully regulated, and the preparations of bismuth, together with small doses of opium, may be administered. Not rarely there is a tendency to constipation which yields to simple salt-and-water enemata or glycerin suppositories.

General asthenia is often marked and persistent. Under these circumstances the patient's activities must be kept well within the limit of fatigue. If cardiac asthenia be pronounced, as shown by feeble, rapid, or irregular pulse and faintness, and dyspnœa upon exertion, carefully regulated rest, alternating with gentle, systematic exercise supervised with equal care, an abundant, nutritious dietary, together with strychnia, arsenic, and iron, prove useful. Alcohol is also indicated. These measures constitute also the proper treatment of the associated anæmia. Early change of surroundings and climate is of advantage.

The falling of the hair that takes place during convalescence is in the majority of instances followed by a new growth. Experience has shown that it is undesirable to subject the patient to the annoyance of shaving the head, though the hair should be cropped close to the scalp.

Under favorable conditions the convalescent from enteric fever rapidly gains in weight; he gains strength more slowly.

The *furunculosis* of convalescence is to be treated by the prompt evacuation of the pus, the application of antiseptic dressings, and in persistent cases the internal administration of calcium sulphide.

Periostitis occasionally occurs. Exceptionally the inflammation undergoes resolution without the formation of pus; more commonly suppuration occurs and extensive necrosis may take place. Early surgical treatment is indicated.

Peripheral neuritis, which affects more frequently the lower extremities, is to be treated by rest, massage, and electricity, together with the use of cod-liver oil, iron, and minute doses of arsenic.

Persistent rhachialgia and other spinal symptoms are best treated by rest, massage, and the occasional application of the Paquelin cautery. In some of the reported cases suggestion appears to have played an important part in the rapid amelioration of the symptoms.

Thrombosis of the femoral vein should be treated by the application of a flannel bandage from the toes to the groin, the elevation of the foot and leg upon a pillow, and the control of the early pain by hypodermic injections of morphia. After a sufficient time for the complete organization of the thrombus has elapsed the establishment of a collateral circulation may be favored by daily massage. When pain and tenderness have disappeared and the patient is sufficiently convalescent to leave his bed, an elastic stocking should be worn.

(*e*) **Specific or Etiological Plans of Treatment.**—Quinine, calomel, iodine, carbolic acid, sulphurous acid, chlorine, salol, boric acid, turpentine, oil of eucalyptus, thymol, camphor, the naphtols and naphtalin, bismuth salicylate, guaiacol, and many other drugs have been administered on theoretical grounds to patients suffering from enteric fever. The temporary administration of certain drugs of this class may have in some instances exerted a favorable symptomatic influence upon the gastro-intestinal derangements of the disease. There is, however, no adequate evidence to show that any of them or any combination of them, persistently administered throughout the course of the attack, is capable of any definite favorable modification of the toxæmia or of uniformly abridging the duration of the attack or notably reducing the death-rate in large series of cases. None of these drugs can be said to have stood the test of time in the treatment of enteric fever or to have been generally adopted by the profession.

Intestinal antisepsis, in so far as the pathogenic organisms of enteric fever are concerned, is directed against specific germs not present in the bowel prior to the breaking down of the intestinal lymph elements, and is therefore largely inoperative; general antisepsis, if by that we are to understand a germicidal influence upon bacteriological forms diffusely implanted in the lymph tissues throughout the organism, is a vain fancy, wholly unsupported by facts. The parasite is more resistant to such influences than the host. Clinical and pathological considerations are alike opposed to the whole subject of the antiseptic treatment of enteric fever.

(*f*) **The Method of Hydrotherapy.**—Curry at Liverpool, at the close of the last century, and Nathan Smith of Yale College, about the same time, advocated the use of cold water in the treatment of the more serious symptoms of the fevers. The methods consisted principally in cold affusion, though sponging was also employed. The teachings of these physicians were not generally accepted. It is true that during the past century hydrotherapeutic methods have been employed in the treatment of the fevers, and especially in combating high temperature. Nevertheless, it remained for Ernst Brand of Stettin to formulate a definite procedure for the treatment of enteric fever by systematic cold bathing. Brand's first publication upon this subject appeared in 1861.

The method attracted little attention, however, until about the time of the close of the Franco-Prussian War in 1871. It was subsequently practised in the hospitals at Lyons by the French military surgeons, who as prisoners of war had had the opportunity of observing its effects at Stettin. Its practice has slowly but steadily extended, until it is now extensively employed in hospitals and to some extent also in families. The method of Brand has been continuously used in the German Hospital of Philadelphia since I introduced it in my service there on the 1st of February, 1890. All patients suffering from this disease have been submitted to it except very rare cases in which the axillary temperature has not reached 101.5° F. (38.6° C.), some of those admitted late in the course of the attack—that is, during or after the third week—and those brought in moribund.

The details of the method, which except in some minor particulars is that formulated by Brand, are as follows:

The patient receives a full bath at about the temperature of the ward every three hours when the thermometer placed in the rectum registers 102.2° F. (39° C.) or over. When axillary temperatures are taken the bath is administered at the end of the third hour if the temperature exceed 101.5° F. (38.6° C.). The temperature of the bath standing in the ward varies between 65° and 70° F. (18.3°–21.1° C.); if in very warm weather it be found higher than 70° F. (21.1° C.), it is cooled to that point by ice or the addition of freshly drawn water. Shortly after the patient has fully reacted, usually in half or three quarters of an hour, his temperature is frequently taken again in order to determine the effect of the individual bath. This is not, however, necessary, and is very often omitted, especially if the patient be already asleep. The patient remains in the bath, as a rule, fifteen minutes, during which time he is systematically rubbed by the attendants and encouraged to rub himself. For this purpose the nurses use their bare hands or bath-gloves. These frictions stimulate the peripheral circulation, constantly change the water in contact with particular points of the surface, moderate the sensation of cold, and, as Glénard has remarked, help to pass the time. If the pyrexia be high, the temperature before the bath exceeding 104° F. (40° C.) or rising very rapidly after the bath, or if it be but little influenced by the bath, the immersion is prolonged to twenty or, in unusual cases, to twenty-one or twenty-two minutes.

The tub, which is upon wheels, is placed at the side of the bed and parallel to it at the distance of about a yard. Both are surrounded by ward screens of white muslin upon iron frames, leaving sufficient room for the attendants. The patient's night-dress is removed under the bed-covering, his body is covered with a sheet or a large folded napkin is placed about the loins, and he is lifted from the bed into the bath. Many of the patients in whom the treatment is instituted early in the attack, or in whom for other reasons the symptoms are comparatively mild, prefer to rise and step into the tub with the assistance of the attendants, and no harm has ever been observed to result from permitting them to do so. If the patient be asleep, he is not immediately bathed, but fifteen or twenty minutes are permitted to elapse after he is aroused. If he be sweating, his skin is thoroughly dried before the bath. The tub is lined with planished copper, perfectly smooth. There is a sloping support for the shoulders and head of the patient, which, however, rest upon a rubber air-cushion. The water, usually about thirty gallons for the adult, is sufficient to cover the patient to the neck. Upon entering the bath he receives an ounce of spirit well diluted or half a glass of red wine, or either of these may be administered in divided amounts during the bath. His head and face are immediately and repeatedly bathed with cold water, and a compress wet with the same is applied to his forehead; a basin and pitcher of cold water are at hand for this purpose. In cases with high temperature or marked nervous symptoms the cold water is very often from time to time poured over the head and face from the height of a few inches.

Upon entering the bath the respirations are suddenly deepened. After the first shock the sensations for a time are not disagreeable, but in five or six minutes the patient begins to be restless and complains of cold. In ten or twelve minutes shivering takes place. About the same time the extremities and face become slightly cyanotic. While the patient is in the bath his bed is covered with a rubber sheet, this with a blanket, and over both is laid an ordinary ward sheet. The patient is lifted out, laid upon the bed thus arranged, closely tucked in the sheet, and covered with the blanket. In the course of ten or fifteen minutes he is thoroughly dried and his night-dress is replaced. About this time reaction is usually established, the patient receives nourishment in the form of milk or broth, and quickly falls into a gentle sleep. When there is marked cardiac asthenia or if for any other cause reaction is retarded, the patient should be at once dried beneath the blanket, receive a hot toddy, and have a hot water bag placed in contact with his feet. The condition of the patient is carefully watched during the bath, and its duration is shortened if its immediate effects, as manifested by shivering, cyanosis, and restlessness, are too pronounced.

The German Hospital has a wheeled tub for each of the small wards set apart for the enteric fever cases. Several forms of portable tubs are supplied by dealers. An ordinary tub may be placed upon a low truck or platform upon wheels. In private practice the portable tub of Dr. Batt is convenient for immediate use.[1] There is no difficulty, however, in procuring an ordinary tub from a plumber, which may remain permanently by the bedside of the patient, being noiselessly and with but little trouble filled by means of rubber tubing from the faucet in the neighboring bath-room, and emptied by the same tube used as a siphon out at the window or into a basin connecting with the drainage system of the house upon the floor below.

In the fever wards of the German Hospital the tubs are filled directly from a tap of sufficient length extending from the wall at a proper height, and they are emptied at the same point directly into a waste-way in the floor, the wall and floor being lined with slate or tiling.

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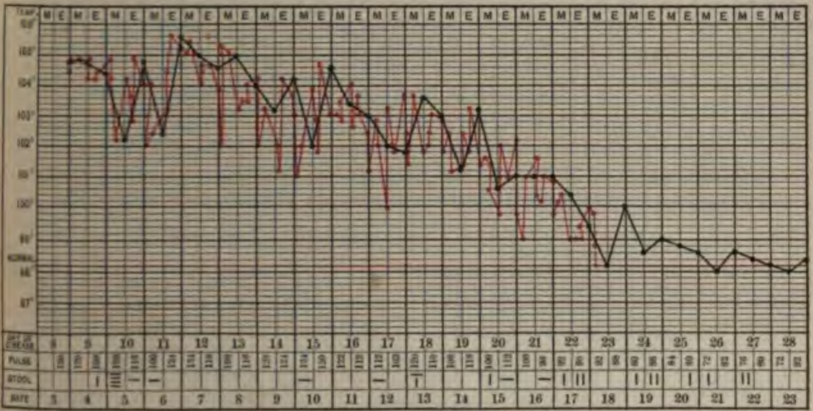
[1] Dimensions of tub when ready for use: length, 6 feet 3 inches,; width, 22 inches; depth, 18 inches. Dimensions of tub when folded for carrying: length, 2 feet 9 inches; thickness, 9 inches. Dimensions of box containing frame: length, 3 feet 3 inches; width, 8 inches; depth, 3 inches.

The tub part is composed of heavy canvas covered with rubber, is seamless, and has a tensile strength of 350 pounds. The tub is supported by hooks inserted through the canvas before the rubber is applied. The frame is composed of brass pipe nickel plated. Both tub and frame can be rendered aseptic by boiling.

For a single patient, as occurs usually in private practice, the water should be changed once in twenty-four hours. In hospital practice, especially when a number of cases are being treated, it becomes necessary to bathe several patients in the same water. After the sixth bath the water should be changed. The patients void urine always immediately before the bath, and I have never known an instance in which fecal incontinence occurred during the bath. It is desirable to have two attendants for the administration of the bath, though under ordinary circumstances, when the patients are in a condition to assist themselves, the bath may be administered by a single attendant. When there are a large number of cases in hospital wards, as frequently occurs at the time of the epidemic prevalence of the disease, the administration of the baths becomes very laborious and a correspondingly large staff of nurses is required. During the bath the temperature of the water is slightly raised, the change amounting to from 2° to 3° F. (1.1° to 1.6° C.). The frequency of the bath is determined by the effect upon the patient's temperature. If at the end of three hours the temperature remains below 101.5° F. (38.6° C.) in the axilla or 102.2° F. (39° C.) in the rectum, the patient is not disturbed until his temperature is again taken at the end of another period of three hours. If, however, during the second period of three hours nervous symptoms arise or manifest increase of fever is present, the temperature is taken sooner and the bath administered at once according to rule. Milder cases and those with declining temperature may require only two or three baths in the course of the twenty-four hours. Early cases and those with high temperature are subjected to the bath every third hour, alike during the day and night, and it sometimes happens that these frequent baths are necessary for several days in succession.

FIG. 24.

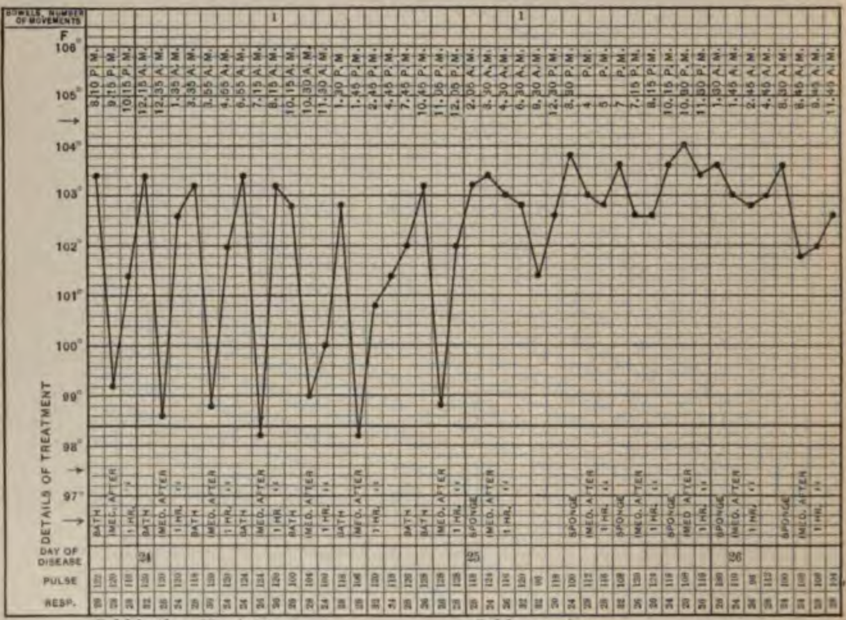


Case bathed from ninth day. The black line shows A. M. and P. M. temperatures; the red line the third hour temperature taken immediately before the baths (German Hospital).

Patients admitted prior to the tenth day of the attack receive one or more laxative doses of calomel. Other drugs are ordinarily not administered, and a majority of the patients reach convalescence without a single further dose of medicine. The maxim that the patient rather than the disease is to be treated is, however, constantly borne in mind, and when the indications have arisen I have not hesitated to administer increased doses of alcohol and aromatic spirit of ammonia, strychnine, opium, etc. in full doses. The necessity for medication has, however, in my own service been very infrequent.

The *diet* has been already detailed. It has not only been possible to give it in larger amounts than under the ordinary expectant method of treatment, but patients frequently crave and demand food throughout the attack. In such cases two or more raw eggs are added to the milk and broth ordinarily administered. During convalescence red wine and

FIG. 25.



Enteric fever, showing immediate effects of individual baths upon the temperature, and rapid rise to the fastigium; also slight effects of cold sponging (Pennsylvania Hospital).

preparations of iron, especially Basham's mixture of iron and ammonium acetate, are administered. No solid food is given until the evening temperature has been normal for a week.

Brand has shown that the mortality is reduced to a minimum where the treatment is instituted prior to the fifth day. A diagnosis of enteric fever can rarely be made in civil practice so early as this. The regular daily system of personal inspection and reports in military practice render a probable diagnosis practicable thus early. In hospital practice a small proportion only of the cases are admitted during the first week. In the service of the German Hospital a provisional diagnosis of enteric fever is regarded as an indication for the employment of the baths upon admission. Under this practice occasional errors have led us to bathe patients who have subsequently proved to be suffering from influenza or other acute febrile disease.

As a rule, the beginning of the attack can only be approximately fixed. The clerks are instructed in taking the histories to date the beginning of the attack from the day on which the patient regarded himself as having fever or on which he was obliged to give up work. The eruption and enlargement of the spleen are events that aid in fixing the period of onset.

In a series of 128 consecutive cases in which the date of the first day of the disease could be approximately fixed we found that of 32 cases admitted not later than the fifth day, 1, or about 3.4 per cent., terminated fatally; of 78 cases admitted prior to the tenth day, 6 died—a death-rate of 7.7 per cent.; and in 18 cases admitted after the tenth day, 4 died, giving a mortality of 22 per cent.

When the diagnosis of enteric fever is clear, neither age, sex, menstruation, pregnancy, nor the free sweating that attends many cases is regarded as a contraindication for the systematic treatment by cold baths or as calling for any modification of this treatment. I have administered the baths at once to patients admitted with broncho-pneumonia or croupous pneumonia as complications, and have continued the treatment when these complications have subsequently developed. The occurrence of intestinal hemorrhage renders the immediate discontinuance of the bath necessary, and in some instances the baths have not been resumed. The signs of peritonitis preclude the administration of further baths. Under this method of treatment diarrhœa is rarely a troublesome symptom: if the stools number more than three or four in the course of twenty-four hours, large cold water compresses or ice-bags are applied to the surface of the abdomen in the intervals between the baths. Constipation has been usually readily relieved by enemata.

When the temperature no longer rises above 101.5° F. (38.6° C.) no further baths are administered and the patient is regarded as entering upon convalescence. He is kept in bed and upon a liquid diet until the evening temperature has been normal for a week. He is then allowed to spend a portion of the day in a chair, and after a time is allowed to walk about, and in suitable weather to go into the open air. In uncomplicated cases the convalescence is usually more rapid than after other methods of treatment, and most of our patients in the German Hospital have returned to their homes within a fortnight of the completion of the defervescence.

The treatment of enteric fever by systematic cold bathing constitutes a definite procedure not to be confounded with other hydrotherapeutic measures, such as the cold pack, cold affusions, spraying, or continuous immersion. It is to be looked upon as a method entirely distinct and different from any form of merely antipyretic treatment. The reduction in temperature by the individual bath constitutes one only of several important effects of the routine, systematic, rhythmical use of the bath at regular intervals. In a majority of the cases after six or eight baths have been administered a striking modification of the clinical picture takes place. Headache, delirium, and stupor cease; the patient falls into natural sleep, from which he is easily aroused, often with a bright expression and clear mind; tremor and subsultus are not often seen;

the tongue cleans off and becomes moist; anorexia becomes less marked, and it is not uncommon even in the midst of the attack for the patient to take his food with avidity; tympanites is rarely seen, and excessive or troublesome diarrhœa is exceptional. In a series of 140 of our cases at the German Hospital intestinal hemorrhage occurred in 10 instances, or 7 per cent.

The effect upon the circulatory system is distinctly favorable. The deep inspirations immediately following the immersion of the patient, and from time to time excited by the application of cold water to his face, neck, and the upper part of his chest during the bath, tend to diminish the danger of pulmonary complications, to fully expand the peripheral vesicles, and to prevent hypostasis.

The influence upon the circulatory system is immediate and marked. Shortly after immersion the pulse becomes smaller, its tension is increased, its frequency reduced—dicrotism ceases. These effects upon the respiration and circulation are maintained for some time after the patient has been taken out of the bath and put to bed. In severe cases, and in particular in those in which the treatment has been instituted comparatively late in the course of the attack, symptoms of collapse may occur. Under these circumstances the duration of the bath must be reduced to five or even three minutes, and in rare instances it becomes necessary to abandon the treatment altogether.

The secretion of urine is increased. Slight transient albuminuria without casts is occasionally observed. Nephritis does not appear to be more common as a complication than under other methods of treatment.

The effect of the individual bath upon the fever is decided, the fall of the temperature, as taken in the rectum fifteen minutes after the bath, ranging from 1° to 4° F. (.55°–2.2° C.). In some instances the reduction is even greater than this. This abrupt fall is usually followed by a gradual rise, the fastigium being regained at the expiration of two or three hours. The effect of the single bath upon the temperature is much less and the succeeding rise is more rapid in the early than in the later course of the attack. In some instances the effect of the bath upon the temperature remains for several days slight; more frequently decided falls and more gradual rises are observed after a series of six to ten baths have been administered. In children the reduction of temperature is greater and more rapid than in adults. A striking modification of the general temperature curve is shown in the form of the lysis, which is usually prolonged and gradual, covering a period of eight or ten days from the end of the second week, and contrasting strongly with the remittent fever curve of this period of the attack under ordinary methods of treatment. In the milder cases the course of the attack is shortened; in those of average intensity and severe cases it does not appear to be abridged. Convalescence, however, is shortened and sequels are comparatively infrequent. In 408 cases treated in the German Hospital according to this plan up to October 1, 1894, relapses occurred in 46 instances—11.3 per cent.—and more than one relapse in 2 instances. The general statistics of the bath treatment show a higher proportion of relapses than those of other methods. It has been suggested that the increased frequency of relapse may be related to the diminished death rate.

The influence of this method of treatment upon the death rate is decided, and there is a remarkable correspondence in the statistics of different observers. Thus, the mortality in the Red Cross Hospital at Lyons, according to Tripier and Bouveret, amounted to 7.3 per cent.; that of F. E. Hare in the Brisbane Hospital, Queensland, 7.84 per cent.; that of Osler in the Johns Hopkins Hospital, 7.1 per cent.; that at the German Hospital in Philadelphia to 7.8 per cent.[1] These results demonstrate that the method of Brand, systematically carried out and applied to successive cases as they present themselves, effects a reduction in the death rate of more than 7 per cent. The fatal cases under this method of treatment have, as a rule, been grave from the beginning, though death has very often not occurred until after prolonged illness. In some of them the evidences of an intense local or systemic infection, such as intestinal hemorrhage, perforation, and very high temperatures, have been present. In others grave complications, such as pneumonia, acute nephritis, and meningitis, have occurred. Finally, a small proportion have died in relapse.

Much has been written concerning the harshness of the Brand method of treating enteric fever. It has been criticised as "brutal" and "barbarous." Our experience at the German Hospital does not justify these criticisms. It is true that the patients very often complain of the disagreeable sensations attending the earlier baths. After a day or two they become accustomed to them, and it has happened in more than one instance that the patient has stepped into the tub at his bedside without waiting for the nurse. Occasionally the patients have complained of the baths throughout the whole treatment. In private practice I have sometimes found very great difficulty in overcoming the objections of the patient, but in no instance have I been forced to abandon the treatment on this account. The treatment involves discomfort and occasionally some suffering upon the part of the patient, and entails upon the nurses and attendants a vastly increased amount of labor, especially in hospital practice, where there are at times a large number of cases to be cared for. These facts cannot be disregarded, but they are without weight as objections to a method of treatment which diminishes the sufferings of the individual and reduces the general mortality at least one half.

(*g*) **Prophylactic and Curative Inoculations.**—The investigations of Stern, Brieger, Kitasato, and Wassermann led Fränkel and Manchot to employ in the treatment of cases of enteric fever a sterilized liquid obtained from the culture of typhoid bacilli in bouillon made from the thymus of the calf and heated to 60° C. Their report is based upon the employment of this procedure in 57 cases. Injections were made deeply into the muscles of the buttock, and were without unfavorable local effects. The first injection consisted of 0.5 c.c. of the sterilized fluid, and was not followed by reaction even in the case of children. On the following day 1 c.c. was injected into the opposite buttock. The second injection was followed in the majority of cases by rise of temperature with chilly sensations. In the course of some hours the temperature usually showed a decided fall, but rose again in those cases in which the injections were discontinued. Fränkel administered the injections every second day, increasing the dose 1 c.c. each day. The temperature range ceased to be subcontinuous and showed marked remissions. Constitutional symptoms were less intense, and complete absence of fever resulted in the course of a few days. The early defervescence was followed by diuresis with cessation of diarrhœa. The spleen remained enlarged and rose spots persisted.

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[1] Further statistics of the German Hospital to January 1, 1896, are as follows:

From October 1, 1894, to January 1, 1895, 27 cases with 5 deaths; mortality, 18.5 per cent.

January 1, 1895, to January 1, 1896, 90 cases, 89 treated by baths, with a single death; a mortality of 1.1 per cent. The fatal case among the bathed cases in this series was that of M. H——, female, single, aged twenty-five, a native of Germany. Death occurred during the third week of the disease from peritonitis following perforation of the intestine. The fatal case not bathed was that of H. S——, male, white, aged twenty-seven, unmarried, a carpenter. This patient was admitted to the hospital in the afternoon of October 14, 1895, having been sick only a few days. He was suffering from convulsions; temperature, 102.7° F. (39.3° C.). Died the following morning. The anatomical diagnosis, based upon the intestinal lesions, together with enlargement of the spleen and of the mesenteric glands, was enteric fever.

The total number of cases treated by systematic cold bathing to January 1, 1896, is 524, with 38 deaths; a mortality of 7.25 per cent.

Rumpf about the same time published the results of the treatment of 30 cases of enteric fever with sterilized cultures of the bacillus pyocyaneus. The fluid employed was obtained by the culture of the bacillus pyocyaneus in thymus bouillon. Its action was very much like that observed in the cases treated by Fränkel with typhoid bouillon. The temperature curve shortly assumed the remittent type; diuresis occurred, together with rapid subsidence of nervous symptoms.

Hammerschlag has reported 5 cases of enteric fever treated by the transfusion of blood from convalescent cases. The results, however, are inconclusive. Hughes and Carter treated several cases with blood serum obtained from convalescents. In some instances the injections were followed by a decided fall of temperature. Otherwise there was no important modification of the symptoms.

Beumer and Peiper employed 1 per cent. peptone bouillon as a culture medium, and destroyed the bacilli by exposure to a temperature between 55° and 60° C. for one hour. Longer exposure or a higher temperature decidedly decreased the virulence of the culture. Sheep were inoculated with these cultures at intervals varying from three days to two weeks, the amount injected being gradually increased from 1 c.c. to 100 c.c. The animals were then bled, the serum treated with 0.5 per cent. solution of carbolic acid, and preserved in a cold, dark place. Serum obtained from uninoculated sheep was found to be unfavorable to the development of bacilli typhi abdominalis, but the serum from inoculated sheep was far more unfavorable to their development. This serum was found to possess both immunizing and curative properties. No dangerous effects followed its injection in healthy men, but further experimentation is necessary to establish its immunizing and curative effects in the human being.

Klemperer and Levy by treating dogs with gradually increasing amounts of bouillon cultures of typhoid bacilli obtained a blood serum capable of immunizing susceptible animals, such as mice and guinea-pigs, against the action of virulent typhoid bacilli, and of effecting a cure by this treatment some time after infection had been produced. They established the fact that the administration of the serum in small quantities to human beings was without danger. The treatment was thereupon instituted in 5 patients suffering from enteric fever. Three injections were administered upon successive evenings. No local discomfort or constitutional disturbance resulted. Neither cutaneous rashes nor albuminuria followed. The patients were selected cases in the first week of the attack, the subsequent course of which was mild.

TYPHUS FEVER.

By ALVAH H. DOTY, M.D.

Definition.—Typhus fever is an acute, characteristic, infectious and essential fever. It prevails in this country only in an epidemic form. No affection runs a more defined and limited course; an abrupt change (crisis) takes place on or about the fourteenth day. Eruption is almost always present, and constitutes the sign by which the disease can usually be recognized; without it a positive diagnosis cannot be made.

History.—Typhus fever is unquestionably a disease of antiquity; excellent descriptions of it are given in the works of the earliest medical writers. It seems strange that a malady which in times past has decimated not only armies, but countries, should not have been better understood and its identity sooner established. It had long been regarded, however, as a variety of continued fever which at times appeared in an epidemic form, and apparently but little effort was made to separate it from other diseases with which it was confounded. It is certain that little attention was paid to its infectious character. During the epidemic of typhus fever which occurred in Philadelphia in the year 1836, Drs. Gerald and Pennock of that city, after careful and exhaustive study, were convinced of the non-identity of typhus and typhoid fevers. Their conclusions were afterward confirmed (1849–51) by the very valuable clinical and pathological investigations of Sir William Jenner in the London Fever Hospital. The devastation caused by this disease in early times was in a great measure due to the non-recognition of its infectious character and the want of proper precautions to prevent its propagation.

Synonyms.—During the long period in which confusion reigned concerning the nature of typhus fever it received innumerable names, suggested by different symptoms and signs which are more or less constant in this disease, or by its occurrence in certain localities or under certain circumstances. Among the more common designations found are ship, jail, camp, malignant, spotted, pestilential, and pyogenic fever, Irish ague, and the plague. These various names, although still used by some, are manifestly improper and should be discarded. The doubt and uncertainty existing in the medical profession before 1840 regarding typhus fever are well indicated by the above array of names.

The term typhus was probably suggested by Boissier de Sauvages in 1760. It is not a fortunate one, as it refers simply to the clouded condition of the mind which is so marked in this disease; nevertheless, custom has confirmed its use, and it will probably be retained.

Etiology.—*Typhus Bacillus.*—Whatever may have been the former opinion as to the origin of typhus fever, it may be regarded as settled that it is caused by a specific living micro-organism. The fact that the specific organism has not yet been identified should not militate against this conclusion. Clinical observation in this disease, in conjunction with our present knowledge of the germ origin of the infectious diseases, leaves no reasonable doubt as to the manner by which typhus fever is propagated. The statement that the specific organism of typhus fever has not thus far been discovered is not meant to imply that numerous and careful investigations have not been made. Hlava states that during an epidemic at Prague in the year 1888 he found in the blood of 20 out of 23 cases of typhus fever where post-mortem examinations were held, and in 2 out of 10 cases examined during life, a well defined bacterium to which he has given the name of *Streptobacillus*. He believes this to be the cause of typhus fever. It was found only in the blood. Injections of cultures of this organism into mice, rabbits, cats, and pigeons were followed by negative results; some febrile reaction was produced in young pigs. Hallier, Zuelzer, Thoinot, Calmette, Mott, Lewaschen, Cheeseman, and others during the past twenty-five years have reported the discovery in the blood of various germs which they believe to be the cause of typhus fever. There is still a want of concert in the results of these investigations, and sufficient evidence has not yet been presented to decide this important question, although there is little doubt that the discovery of the true organism is only a question of time.

Notwithstanding the now generally accepted belief as to the infectious origin of typhus fever, there are those who decline to accept this conclusion and follow the teaching of Murchison, who died in the conviction that it was possible and probable that the disease could be generated *de novo* by the crowding together of many persons in badly ventilated apartments, combined with filth and insufficient food. The disease thus produced he believed was capable of transmission to others. Although this theory cannot be entertained, it should receive the most respectful consideration, coming as it does from one to whom the world is indebted for valuable observations and statistics regarding this disease. It must be remembered that Dr. Murchison died in 1879, when comparatively little was known regarding micro-organisms in relation to disease, and that his study of the subject was limited, his deductions being based solely on the results of his clinical observations. It may be stated that Dr. Cayley, editor of the third edition of Murchison's work on continued fever, endorses the present belief regarding the origin of typhus fever. Murchison was unduly impressed with the fact that typhus fever frequently appeared abruptly in imperfectly constructed camps and in jails and other institutions which were overcrowded and badly ventilated, and in which the inmates were supplied with poor food, and where no apparent source of infection save that due to the unsanitary conditions existed. That this renders the soil favorable for the propagation of typhus fever is beyond dispute, and we are oftentimes baffled in our attempts to ascertain the manner by which the contagium has been introduced into an institution or community. Failing in this, however, we should not infer that the disease is generated *de novo*. Numerous cases have occurred in my own experience where the contagium has been received in a most peculiar and unexpected manner, and the source has only been discovered after long and careful investigation. If the typhus contagium were generated *de novo* when overcrowding, poor ventilation, and poverty are present, we should expect to find it more or less constantly where these conditions exist. Statistics and facts do not show this. Innumerable instances could be cited where all of these factors were present—notably the military prisons during the late war, where personal hygiene, etc. were at their lowest ebb—still, typhus fever did not appear.

PREDISPOSING CAUSES.—Accepting, as we must, the present belief as to the exciting cause of typhus fever, it will be necessary to study the predisposing causes. Foremost among them are *overcrowding*, *poor ventilation*, and *poverty*. As these conditions are mainly confined to the poorer class, we should consequently expect to find the disease principally among these people. This is clearly and strikingly verified. Out of 439 cases of typhus fever which occurred in the city of New York during 1892 and 1893, 434 were removed from the poorer tenement and lodging houses, principally the latter. Of a group of 48 cases removed to the Reception Hospital during the winter of 1881–82, all were from the poorer class of tenement and lodging houses or were inmates of workhouses or hospitals. Of the 18,268 typhus patients admitted to the London Fever Hospital during a period of twenty-three years, 95.76 per cent. belonged to the lowest classes, and were, as a rule, inmates of workhouses, etc. (Murchison).

Famine and *scarcity of food* have commonly been followed by typhus fever. The horrors of the Irish famine which occurred between 1813 and 1818, and which affected the lower classes, can hardly be exaggerated. The intensely cold weather during these years had almost completely destroyed the potato and other crops. For the want of work thousands were rendered homeless and obliged to wander about in quest of food. Innumerable cases of starvation occurred, and, as might be expected, these people were ripe for the reception of typhus fever. The few cases which were constantly occurring in Ireland during the latter part of 1816 rapidly increased, until a terrible epidemic resulted. It is estimated that during this period there were 800,000 cases in Ireland, which represented about one eighth of the entire population. In Dublin alone there were 70,000 cases, representing one third of the whole population of the city. The epidemic disappeared during the latter part of 1819. It is a significant fact that the disappearance followed the abundant harvest of 1818.

Intemperance.—The influence of intemperance on the propagation of typhus fever is marked, and has been recognized by all who have had to do with this disease. More than one half the patients suffering from typhus fever removed to the Reception Hospital in New York City during the epidemics of 1881–82 and 1892–93 were addicted to the immoderate use of alcohol. The statistics of the Glasgow and Edinburgh infirmaries, as cited by Craigie and Davidson, also show that over 50 per cent. of the typhus fever patients admitted to those institutions were intemperate. It will be seen that poverty, intemperance, overcrowding, etc., by interfering with the proper nourishment of the body and with the functions of the different organs, reduce the vital resistance and render a person more susceptible to the typhus contagium, and after receiving it less able to combat it; whereas those who are well nourished, of regular habits, temperate in regard to the use of alcohol, and who live in clean and well ventilated and not overcrowded apartments, are far less susceptible than those in the group above referred to, and offer better prognosis.

Temperature and Season.—Although typhus fever seems to be more readily propagated during the winter months, it cannot be said that temperature or the season of the year has any special influence as a predisposing agent. It is true that epidemics are more apt to occur during the cold weather, particularly during the winter months, but this is unquestionably due to the fact that at these periods the people are kept closer together, ventilation is made imperfect in order to retain as much heat as possible in living apartments, and more poverty exists. As a result of these influences the disease is more readily contracted. There are some countries, such as Ireland and Russia, where the disease is always present. This is undoubtedly due to the manner in which the people live while in their own country, as investigation does not show that they are more susceptible to the disease during the epidemics that have occurred in the United States. Typhus may occur in any country excepting those within the tropics.

Sex and Age.—Sex has very little influence in the propagation of typhus. Of the 18,268 cases reported by Murchison above referred to, 8946 were males, and 9322 were females. This may be regarded as representing about the usual percentage of each sex when both are equally exposed to the infection. Of 741 cases occurring in New York City during the epidemic of 1881–82, there were 632 males and 109 females; during the epidemic of 1892–93, out of 663 cases there were 535 males and 128 females. During both of these epidemics the patients were mainly removed from cheap male lodging houses, while the patients figuring in Murchison's statistics were taken mainly from residences, institutions, etc. where both males and females were inmates.

The following tables, taken from the records of the Riverside and Reception Hospitals, New York City, show the relative frequency of the disease between infancy and old age:

Table showing the Influence of Age.

1881.

Age.	No.	Per cent.
5 years and under,	3	0.57
5 " to 10,	20	3.78
10 " to 20,	51	9.64
20 " to 30,	156	29.49
30 " to 40,	152	28.73
40 " to 50,	83	15.69
50 " to 60,	41	7.75
60 " to 70,	20	3.78
70 " to 80,	3	0.57

1882.

Age.	No.	Per cent.
5 years and under,	1	0.49
5 " to 10,	5	2.42
10 " to 20,	24	11.65
20 " to 30,	49	23.79
30 " to 40,	63	30.58
40 " to 50,	37	17.96
50 " to 60,	21	10.19
60 " to 70,	5	2.43
70 " to 80,	1	0.49

1892.

Age.	No.	Per cent.
5 years and under,	15	6.69
5 " to 10,	23	10.27
10 " to 20,	62	27.68
20 " to 30,	61	27.23
30 " to 40,	33	14.73
40 " to 50,	22	9.82
50 " to 60,	8	3.58

1893.

Age.	No.	Per cent.
5 years and under,	1	0.23
5 " to 10,	4	0.91
10 " to 20,	22	5.01
20 " to 30,	120	27.33
30 " to 40,	136	30.98
40 " to 50,	92	20.96
50 " to 60,	39	8.88
60 " to 70,	23	5.24
70 " to 80,	2	0.46

Murchison found the mean age of 3456 cases under observation at the London Fever Hospital from 1848 to 1857 to be 29.33 years, " which is about three years above the mean age of the total population." Of 18,138 cases reported by the same author, 16.16 per cent. of the cases were between fifteen and nineteen years of age; 12.6 per cent. were between ten and fourteen years of age; 13.25 per cent. of the cases were between twenty and twenty-four: these are the three largest percentages of this table. A study of the tables taken from the Riverside and Reception Hospitals will show a marked difference in the frequency of typhus fever at different ages. These, however, will be more in harmony with each other when it is understood that during the epidemics of 1881–82 and 1892–93 in the city of New York the disease very early in the epidemic invaded the cheap lodging houses of this city. As these are filled entirely by males, and chiefly by men of ages ranging between twenty and sixty years, with very few boys, it will be appreciated that the cases taken from these places must necessarily be drawn from persons over twenty years of age; whereas in the statistics given from the London Fever Hospital the patients were removed from the cheaper class of tenement houses and residences, where every member of the family was subjected to the same infection. It will be seen, however, that under ten and over sixty-five years of age the disease is infrequent. As already stated, typhus fever is usually mild and rarely fatal under ten years of age.

Other Influences.—Pursuits which involve confinement in close and badly ventilated apartments, or those which entail continued mental excitement or nervous depression, are predisposing agents. Fear is regarded by the laity as a potent predisposing cause. The importance of this is exaggerated, and it probably acts as a predisposing cause only when it impairs the appetite and general health and renders the person extremely nervous. I have met with one well marked instance where fear might be regarded as playing an important part in the production of the disease. It is as follows: An engineer employed on one of the islands under the jurisdiction of the Commissioners of Charities and Correction in New York City became very much frightened when it was announced that typhus fever had appeared in an adjoining building with which he officially had no communication. The man kept religiously away from every one who was in communication with the case, and practically remained in his own apartment when not at work. On the third or fourth day of the outbreak he completely broke down, became violently agitated, and remained in bed, declaring that he knew that he had the fever. The liberal use of bromide, with the assurance that he would not have the disease, put him on his feet again. His work was resumed, but he continued to worry, though physically in good health. During the following week he was taken abruptly ill with typhus fever, and died. While I do not believe that fear can be regarded as an important predisposing cause, I am sure that it militates against recovery if it is well marked, and tends to make a very unfavorable prognosis.

It has been claimed that the typhus germ is lighter than the air: this, however, cannot be accepted as true, and should not be taken into consideration in selecting the apartment for confinement of patients affected with this disease.

Direct contact is not necessary to cause typhus fever. The germ is transmitted by emanations from the body, air-passages, and possibly by discharges from the intestinal tract. Air and fomites act as media in communicating the contagium. Walls and ceilings of apartments become infected. (See *Ventilation*, page 235.) It cannot be estimated how long the contagium remains active under various conditions, and therefore the fact that a long period of time has elapsed since the occurrence of a case cannot, as far as the clothing, bedding, etc. is concerned, be taken in lieu of proper and careful disinfection. It is generally regarded as a fact that the poison must be highly concentrated to be transmitted by fomites. This may be true in the main, but there has been sufficient evidence presented from time to time to prove that a person visiting a typhus case may be the medium by which the disease is carried to other individuals. Sailors have been known to carry the disease to their own ship by having visited infected vessels. A case under my observation in 1893 well illustrates this point: A man living on —— street had died of what afterward proved to be typhus fever. He had before death been removed to the hospital. His apartment in one of the poorer tenement houses had not been disinfected; his wife, desiring to comply with the ordinary custom in these cases, although the body was not present, invited some friends to visit her; among them was a woman, Mrs. M——, living on the Boulevard, who brought with her a friend who lived out of town; the husband of Mrs. M —— was unable to accompany them. After having made a protracted call at the residence of the deceased, they returned home. Within two weeks Mrs. M—— and her husband were removed to the Reception Hospital with typhus fever. The latter, as stated above, did not visit the infected apartment; the germ, it is fair to suppose, was conveyed to the husband by Mrs. M—— and her friend. The latter did not contract the disease.

Attempts have been made to estimate the distance to which the germ may be transmitted; it has been given in feet: this, of course, cannot be entitled to any very serious consideration, as such estimates cannot safely be used in a practical way, since the danger of infection is not dependent alone on the close proximity of the patient. The mixture of plenty of fresh air, which neutralizes the poison by dilution, is an element which is far more important to consider. It is fair to assume that a case of typhus fever in a large and well ventilated apartment will not, as a rule, propagate the disease if a reasonable amount of care is exercised. It is a well known fact that a nurse caring for a case of typhus fever in a private apartment where there is sufficient ventilation runs but little risk of contracting the disease, compared with a nurse who is caring for cases of this kind in the wards of a hospital.

Murchison and Levy believed that typhus is not infectious during the very early period of the disease, probably not until the end of the first week. This belief appears to be rather generally accepted, and I can add that as the result of my personal observation during the epidemics which during the last fifteen years have occurred in New York City I am inclined to endorse this statement. Where patients were removed during the first three or four days of the disease and the apartment was properly disinfected, secondary cases did not, as a rule, occur. Where subsequent cases did occur it is possible and probable that the infection came from some other source. Cases are cited, however, where it is quite clear that the disease may have been contracted during the first days of the disease, and it would be manifestly unsafe to regard this point as in any way settled, as it would necessarily tend to relax our efforts in the prompt removal of cases from tenement houses to other apartments prepared for their reception. It would also interfere with disinfection, the value of which cannot be overestimated. Dr. Moore refers to the opinion of the late Dr. Perry of Glasgow, who believed that the most infectious period of typhus fever is during convalescence. Although this belief is shared by others, I regard its acceptance as dangerous and opposed to the proper protection of the public.

It has not as yet been satisfactorily determined whether or not the dead body is capable of propagating typhus: thus far, there seem to be no well authenticated cases where infection has taken place from this source. Murchison believed that he contracted the disease in the dissecting-room. This, however, could not be substantiated, as an epidemic of typhus fever existed in Edinburgh at the time, and it is but fair to assume that he was brought more or less directly in contact with the disease, and that he was infected in this manner; besides, the clothing which envelops the dead body may be the source of infection. However, as no sufficient reason has been presented why this should not occur, it would be unwise to regard this point as settled.

The question of idiosyncrasy is somewhat obscure, and has about the same relation to this disease as to others. There are some who seem immune to typhus fever and are proof against infection, while others are readily susceptible and may have the disease twice or three times. Dr. Murchison was an example of the latter class, he having had typhus fever twice. What this peculiar susceptibility or immunity consists of is unknown, and cannot be anticipated by an examination of a person.

Does one who is constantly dealing with infectious diseases become immune is a question which is of peculiar interest, but which is seldom referred to. There are those who believe that this is actual, and refer to the small number of cases occurring among health department officials and quarantine officers, who are constantly dealing with this class of disease. It would at least appear to be more than a coincidence. One attack of typhus fever, as a rule, confers immunity against a subsequent one. However, a second or third attack sometimes occurs.

PATHOLOGICAL ANATOMY.—The anatomical changes found after death from typhus fever are not specifically characteristic, but are similar to those present in other acute infectious diseases. The organs present lesions that often occur in various conditions attended with fever, and the most noticeable feature at the autopsy table is the presence of the changes unaccompanied by well marked and specific alterations. The findings at the post-mortem examination, if taken by themselves, apart from a clinical history or a probable exposure to typhus fever, are usually not sufficient to establish the diagnosis.

The skin frequently retains traces of the petechial rash. The blood is generally dark and fluid, and the body tends to early decomposition. The muscles are dark red in color, and may be the seat of granular or waxy changes, and occasionally of hemorrhages. The heart is soft and flabby. The liver is large and soft. The spleen is almost always much enlarged and soft. The kidneys are usually swollen and congested, and the parenchymatous degeneration is more advanced in them than in the other viscera.

The intestines are often normal, but have a rosy color. The Peyer's patches not infrequently present the "shaven beard" appearance, but are never ulcerated as in typhoid fever.

Apart from the parenchymatous degenerations of the organs already mentioned, the most constant complicating lesions are found in the respiratory tract. Acute bronchitis, and pulmonary hypostatic congestion, and œdema are common. Laryngitis and lobular or lobar pneumonia and gangrene of the lungs are sometimes met with.

Inflammations of the serous membranes are very unusual.

INCUBATION.—This period generally ranges from eight to twelve days, usually the latter. There is some diversity of opinion among writers regarding this stage. Hutchison refers to a case where the incubation was thirty-one days. Huss at Stockholm speaks of this stage as one, two, or three days, sometimes ten, or in some cases only a few hours. Lebut in his article on typhus in *Von Ziemssen's Encyclopedia* places it at five to seven days. Where a clear history could be obtained in the cases of typhus fever occurring in the city of New York during 1881–82 and 1892–93 the period of incubation was found to be about twelve days. This, I believe, will prove to be about the duration in most cases if the histories are carefully investigated. I can account for the statements that the usual period of incubation is from three to seven days only on the assumption that the histories of the individual cases were not carefully and fully obtained. While there are very few instances in which the period of incubation exceeds twelve days, there are some where the time is much shorter. Well authenticated cases are even cited in which the period of incubation was hardly appreciated, the stage of invasion occurring almost immediately after the exposure. This may be attributed to a peculiar susceptibility of the individual or to concentration of the poison to such an extent that its effect upon the system was almost immediate. After examining a number of cases of typhus fever I have frequently experienced a headache which has lasted for a portion of the day. This experience has been shared by my colleagues.

SYMPTOMS.—*Invasion.*—One of the marked characteristic signs of typhus fever is the abruptness of its invasion. This can be relied upon as one of the most valuable aids in making an early diagnosis, and is in marked contrast with the slow invasion of typhoid fever.

The period of invasion usually lasts from one to three days, during which the patient suffers from a slight chill or chilly sensations (a decided or well marked chill is unusual): this symptom is accompanied by general malaise, which soon amounts to great and indescribable prostration, accompanied by headache, vertigo, loss of appetite, and soreness about the body; pains in back and limbs, particularly the thighs and calves of the legs. The tongue has a white coating at first, and is usually large and pale. The coating subsequently becomes darker in color. The uniform and well marked congestion of the conjunctivæ peculiar to this disease may be very early recognized, and is a strong diagnostic point in favor of typhus. The dusky appearance of the face is very noticeable. Considerable tremor in the hands is usually present. The urine is high colored, scanty, and may have a specific gravity as high as 1030. There are no special abdominal symptoms; the bowels are usually constipated. There is sometimes nausea, but seldom vomiting. The mental condition becomes rapidly blunted and confused, and the patient is listless and suffers from insomnia. The prostration becomes more marked as the disease passes into the eruptive stage. During the stage of invasion the pulse is increased in frequency and is compressible, and the temperature usually reaches 102° or 103° F., or sometimes even higher.

Eruption.—Usually on the fourth day, rarely after the sixth, the eruption peculiar to typhus fever appears. At first it does not show its true characteristics, but develops as a rash which frequently resembles that of measles and is often mistaken for it. The spots are irregular in form and slightly raised, varying in size from that of a large pea to the point of a pencil. The spots may be isolated or grouped in patches similar to those of measles; they do not at this time present the dusky appearance which is subsequently shown, but have a dark pink color and disappear on pressure. The eruption appears at first on the chest, abdomen, and then on the arms and thighs. The upper and anterior part of the shoulder and the anterior aspect of the forearm have always appeared to me to offer the best aspect for study. At these sites the skin is cleaner and whiter, and the eruption is usually well marked. Some writers lay great stress on the appearance of the eruption on the back of the hand: I do not regard this site as so favorable for study, as this part of the hand, particularly in the subjects who are affected with typhus, is usually hardened and discolored by work and exposure to the weather, and the eruption is not always easily distinguished.

The eruption is not often apparent on the face and neck. Dr. Moore believes this to be due to two reasons: first, because these parts are very vascular and the hyperæmia due to the fever conceals the spots; second, because the rash develops less thoroughly in parts exposed to the air. This explanation appears to be reasonably consistent with the facts as far as it is ascribed to hyperæmia, which in this disease is usually intense. The second reason can hardly be accepted, as in other eruptive diseases, such as measles and smallpox, the eruption on the face is more intense than elsewhere. In addition to the early measly rash referred to, there is often a mottled condition of the skin which is due to a subcuticular eruption. This has the appearance of being deep seated, and, although it can be recognized, it is paler and not as distinct as the former. The "mulberry rash" of Sir William Jenner represents the combination of the two eruptions just described. The mottling is perhaps best seen when standing three or four feet away from the patient. If possible a suspected case of typhus should always be examined in the daylight.

The measly or morbilliform eruption gradually changes its character: the slight elevation disappears, and the dusky pink color becomes much darker, and does not disappear on pressure. This change is constant, and is a very important point in the diagnosis. It is due to capillary hemorrhage followed by the formation of pigment, which takes the place of the very early hyperæmia: this change is fully apparent on the fifth or sixth day, and may be considered the typical and permanent eruption of typhus fever. Another element is to be added to this eruption before its description is complete: I refer to the appearance of true petechiæ, which may be found on the eighth or tenth day in the centre of the dusky spots, constituting the permanent eruption already referred to; they are of a bluish tint and their borders are not abrupt, but grade into the dusky color of the typhus rash; they may involve but a minute portion of the typhus spot or they may almost entirely obscure it. These petechial points represent subcutaneous ecchymoses. The petechiæ alone frequently occur in other diseases; they constitute an extremely important diagnostic sign only when they occur in combination with the dusky rash just described. Credit is given by Murchison to Staberoh, Stewart, and Jenner for the description of the conversion of the permanent typhus eruption into petechiæ. The petechiæ of typhus are, as a rule, confined to adult patients. About the time that the rash is fully formed the subcutaneous eruption or mottling commonly disappears. As might be expected from the description just given of the permanent eruption, it can be recognized after death, provided dissolution does not occur late in the course of the disease from some sequelæ. The eruption generally disappears when about eight or ten days old.

The rash would probably not be present if death occurred on the first or second day of the eruption, while it is due to simple hyperæmia. I know of no statistics regarding this point, as a fatal result rarely occurs at this stage.

As already stated, the typhus eruption never appears in successive crops, as in typhoid fever; a day or two may elapse before the entire eruption presents itself, but when fully out it remains until it all gradually disappears. This is in marked contrast with typhoid fever.

In some cases where the measly or early eruption has been quite prominent a slight desquamation may subsequently take place. This, however, is not very common.

The eruption is almost always present in typhus fever, and without it a diagnosis of this disease can rarely be made. It certainly cannot be made in isolated cases. I have seen but one case where the diagnosis of typhus fever without an eruption was in a measure justified. During the last epidemic in New York City (1892–93) a suspicious case was reported at Mt. Sinai Hospital. The patient, a man, had been removed from a vicinity where typhus fever was prevalent; his temperature and general symptoms were characteristic, but there was an entire absence of an eruption or mottling, the skin presenting a particularly clear and white appearance. The temperature dropped about the end of the second week, convalescence ensued, and the patient was discharged. I saw the case in consultation with Drs. Janeway and Jacobi. The general symptoms, particularly those referable to the nervous system, were characteristic of typhus, and, as there was nothing to account for them, the case was regarded as probable typhus without an eruption. I regard this as justifiable when well marked cases of typhus fever exist in the same place or vicinity. Murchison's statistics of admissions into the London Fever Hospital, which cover a period of twenty-three years, show that out of 18,268 cases of typhus fever the eruption was present in 17,023, or 93.2 per cent. He admits that in some cases the eruption may have been overlooked, and states that in 1864 unusual care was taken at the London Fever Hospital to ascertain if the eruption was present: during this time it was found in 97.77 per cent. of the cases. The class of people usually affected with typhus are those who pay absolutely no attention to personal hygiene or cleanliness, and a slight eruption is easily overlooked, particularly as the examination of the cases is often superficial, the task being as a rule an unsavory one. The eruption is more often absent in children than in adults.

The eruption does not always follow the course above described; it may not pass beyond the first or second stage. In children it usually does not become petechial, and the disease is frequently mistaken for measles. In mild cases the eruption may begin to fade on the third or fourth day.

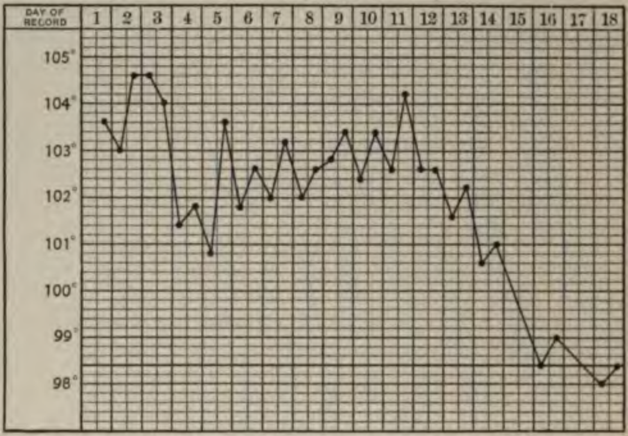
In some few cases the true typhus eruption may be preceded by a preliminary eruption or roseola, which may cover considerable portions of the body and may be confounded with scarlatina. This roseola is transient and gradually fades as the regular eruption appears. It is well to bear this in mind, as a diagnosis of scarlet fever might cause considerable embarrassment and dangerous infection. Dr. Wilks refers to a case where a preliminary eruption covered the whole body, and was undoubtedly promptly diagnosticated as scarlet fever. The appearance of the eruption is not followed by a fall in the temperature, as in the case of smallpox.

Temperature.—There appears to be a uniformity of opinion regarding the character of the temperature in typhus fever. The disease is ushered in with a comparatively sudden rise, which reaches the maximum during the first week or possibly later. It may reach 103° F. on the evening of the first day, rarely rising higher. Murchison had the record of a case which reached 104.9° F. on the first day, as cited by Griesinger. The maximum when reached is generally no higher than 105° F. and a fraction. In children it may reach or exceed the maximum just given without indicating a grave prognosis. A remission usually occurs during the early part of the second week, and in uncomplicated cases a gradual decline takes place until about the fourteenth day, when there is usually a sudden descent of from three to five degrees, to or below normal, commonly the latter. This rapid decline may be immediately preceded by an exacerbation. The sudden decline which occurs on or about the fourteenth day may be looked upon as peculiar to typhus fever: it represents the crisis, and is an exceedingly important diagnostic point. An absence of the remission during the early part of the second week renders the prognosis unfavorable. An increase in the temperature during the second week usually indicates the presence of some complication which is generally referable to the lungs. A low temperature should not afford one a sense of security, as in many fatal cases the temperature does not exceed 103° F. This condition is found where there is a great depression of the vital powers.

The peculiar manifestation of the temperature of typhus fever which is in marked contrast with that of typhoid fever is the slight variation in the daily range. This may be looked upon as the rule, and is exceedingly important in the differential diagnosis. A slight increase in temperature usually occurs in the evening, although in some cases it may be highest in the morning. During the early part of convalesc it frequently remains subnormal. During this period (convalescen temporary rise of temperature may occur without apparent cause without special significance.

The following temperature charts, taken from the records of Riverside Hospital, illustrate the range of temperature in what be regarded as typical cases:

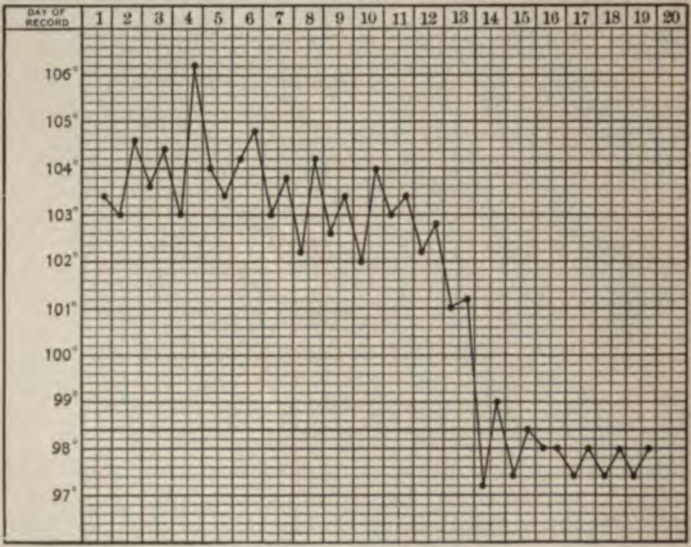
Fig. 26.



Case I.—Temperature chart.

Case I. (recovery).—H. M——, male, aged thirty-two years, wa orderly in the typhus ward of the hospital during the epidemic in York City in 1881. The chart therefore records the range of tem ature from the beginning of the disease.

Fig. 27.

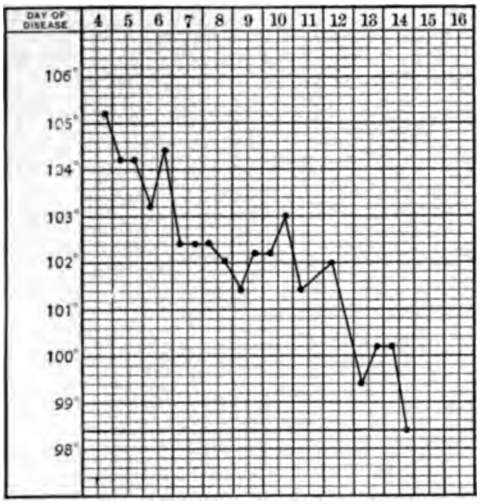


Case II.—Temperature chart.

Case II. (recovery).—J. D——, male, aged eleven years, inmate in an institution in New York City where an outbreak of typhus occurred in November, 1881. The patient was at once removed to the Riverside Hospital.

Case III. (recovery).—G. S——, male aged twenty-six years, Riverside Hospital, February, 1893. The temperature chart in this case indicates the range from the fourth day of the disease. A record of the preceding days was unfortunately not kept, the patient not being under observation.

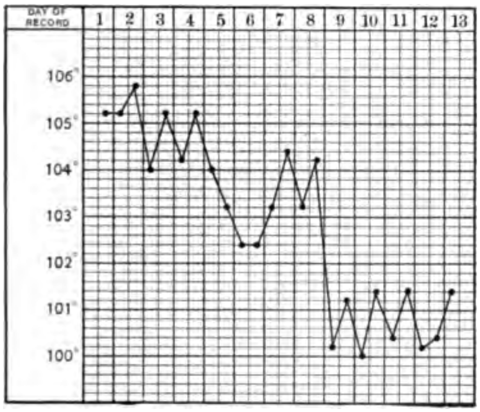
Fig. 28.



Case III.—Temperature chart.

It will be seen by the above charts that the crisis in these cases occurred about the fourteenth day.

Fig. 29.



Case IV.—Temperature chart.

Case IV. (death).—J. C——, male, aged forty-eight years, Riverside Hospital, April, 1893. This patient was an orderly at the Reception Hospital and was addicted to the use of liquor. His death occurred about the fourteenth day of the disease.

Pulse.—The pulse of typhus has certain peculiarities which are generally present in severe and well marked adult cases. In the beginning of the disease it ranges from 100 to 120 or 130. The latter is usually reached on the second or third day. Of 90 cases cited by Murchison, in only 15 did the pulse go above 120. Of 13 cases reported by this author as occurring in the service of Dr. Henderson where the pulse exceeded 134, 5 died. In a group of 26 cases at the Riverside Hospital during 1892–93 between the ages of twenty-one and sixty-five (mean age thirty-seven), there were 10 deaths, in 8 of which the pulse went above 120; of the 16 which recovered, the pulse was above 120 in 6 cases. These patients were inmates of lodging houses, and among them the mortality was high. Dr. Murchison undoubtedly refers to adult cases in speaking of pulse frequency, as it is common to find the pulse above this point (134) in children. In November, 1881, an outbreak of typhus fever occurred among the children who were inmates of an institution in New York City; there were 19 children affected, all under twelve years of age. The records of these cases show that in 10 the pulse was above 130, in 6 it was above 140, and in 3 it was above 150; all of these cases recovered. In the class of severe cases the pulse becomes progressively weaker and the cardiac impulse is finally lost. Subsequently the first sound of the heart becomes weaker and may disappear. The second sound may also be affected in a similar manner. It is very unusual for the pulse to remain firm and strong throughout the first week of the disease. In 90 young and robust patients Murchison found but 4 cases where the heart remained in this condition. During the second week the pulse is usually dicrotic, irregular, or intermittent. During the early part of the disease the pulse rate may be very low, with a subsequent rise. In a case reported by Barallier (Murchison) of a man fifty years of age the pulse remained at 28 for three days. A very low pulse generally denotes extreme prostration.

A stethoscope should be used in ascertaining the condition of the heart and circulation. The radial pulse cannot be depended upon to indicate the number of cardiac contractions, as the heart may beat twice to one wave of the radial pulse. This difference is not only due to feebleness of the circulation, but to a want of muscular tone. In favorable cases the heart becomes somewhat stronger about the tenth or eleventh day. The silence of the heart, as the name implies, means that the pulsations cannot be detected, and almost invariably indicates approaching death. During this period of weakness and rapidity of the heart the daily variation in the number of pulsations is small, a slight increase usually occurring at night. After the first day of the disease there is very little relationship between the temperature and pulse; that is, the temperature may be high when the pulse is slow, and *vice versâ*. During the early part of convalescence the pulse may be slower than normal.

Respiratory System.—The increase in the respiratory action is dependent in a great measure on pulmonary complications; more or less hypostatic congestion is present in nearly all cases. During the first week the respirations do not, as a rule, exceed 25; however, with a high pulse and temperature they may become more rapid. On admission to the hospital of the group of 26 cases above referred to, the number of respirations exceeded 25 in all but 2 cases.

The following table indicates the highest and lowest respiratory range in the 10 fatal cases belonging to this group:

Age. Years.	On admission. Respiration.	Maximum.	Minimum.
21	32	48	28
54	32	56	30
25	44	44	20
42	36	38	22
33	28	34	28
65	30	48	20
35	32	44	26
38	30	54	28
39	26	30	24
55	28	32	18

In the fatal class the mean number of respirations was 43; in the cases which recovered the mean number was 36. The pulmonary congestion usually present may end in œdema of the lungs, which is denoted by hurried and embarrassed respiration; coarse râles at first, then fine crackling râles, and frothy expectoration tinged with blood. This condition usually ends fatally. In cases of great prostration the respirations may be subnormal in frequency and not exceed 8 or 10. In this class of cases the temperature is usually low. In severe cases the respiration may be sighing or irregular. Where great cerebral irritability exists the respirations are jerky and spasmodic. This is regarded by Murchison as an unfavorable sign. The nervous or cerebral breathing of Sir Dominic Corrigan, which is of a blowing or hissing character, and Cheyne-Stokes respiration, are sometimes present.

Epistaxis does not usually occur. In 7000 uncomplicated cases Murchison found it but 12 times. The records of the Riverside Hospital also show that epistaxis is uncommon.

Digestive Tract.—During the first week the tongue becomes very dry and rough. This constitutes a strong diagnostic point in favor of typhus fever, and is present in three fourths of the cases. The whitish fur that is first noticeable changes to a dark brown color, and is generally confined to the centre of the tongue, while the edges and point are pale. This condition continues until convalescence approaches, when the coating gradually disappears and the tongue becomes moist. There is a loss of appetite, and sometimes nausea, but vomiting is uncommon. The iliac meteorism and gurgling which are so often present in typhoid fever are wanting in typhus. Pain or tenderness may be found in the hepatic region, or sometimes in other parts of the abdomen, but it has no particular significance. Constipation is usually present. Diarrhœa sometimes appears at about the time of the crisis.

Urine.—In the early part of the disease the urine is high colored, and may continue so until convalescence is established. It then becomes lighter in color. At first the specific gravity may reach 1030;

this afterward becomes diminished, and is apt to be subnormal after the crisis. The amount of urine at first is notably diminished, even when a large amount of fluid is taken. At this time it usually has an acid reaction. During convalescence the amount is generally equal to or above the normal. Suppression sometimes occurs as the result of an acute nephritis. The chlorides in the urine are markedly diminished, and may disappear as in pneumonia. Investigations by Parke, Murchison, Buchannan, and others show that the urea is at first increased. In a case cited by Buchannan the quantity of urea passed on the fifth day was 851 grains; that passed on the twelfth day was 1011 grains. As a rule, however, the quantity diminishes during the second week, and may fall below the normal register. An increase is also shown in the amount of uric acid. Albumin is probably found in one half or more of the cases. This does not usually indicate previous organic disease of the kidneys, but generally is due to simple hyperæmia or some acute affection of these organs induced by typhus fever. The presence of albumin is frequently accompanied by mucus, epithelium, and casts of the uriniferous tubes. Organic disease of the kidneys renders the prognosis very unfavorable, inasmuch as it favors the occurrence of uræmia and uræmic convulsions.

Nervous System.—Pain in the back and limbs and frontal headache, particularly over the temples, are constant symptoms and are well marked during the first week. The headache was present in almost every case received at the Riverside Hospital during 1881–82 and 1892–93. In 251 cases observed by Murchison and Henderson headache was present in 236. The pain in the different parts referred to varies in intensity, and usually subsides about the seventh or eighth day. At this period deafness, which occurs in a large percentage of the cases, is noticed. This, as a rule, disappears during convalescence or soon afterward, although in a few cases it remains permanent.

Typhus fever is associated with early and great impairment of the mental faculties. Well marked delirium generally occurs during the latter part of the first week, although from the first there is obstinate wakefulness associated with general dulness, the patient being unable to converse intelligently. The delirium occurs at first during the night, but later there is no interval of lucidity. The delirium ranges from a low muttering form, which is so commonly found in older subjects, to that of acute mania, where the patient can only be controlled by force. In alcoholic cases it very frequently assumes the character of delirium tremens. This I have repeatedly noticed in patients removed from lodging houses, these people, as a rule, being alcoholic subjects. A suicidal tendency is not infrequent. The prognosis is in a great measure governed by the degree of delirium; when the latter is profound the prognosis is correspondingly unfavorable.

The pupils are usually contracted, sometimes to an intense degree, producing what is known as the pinhole pupil. The latter condition constitutes a very unfavorable sign.

COMPLICATIONS AND SEQUELÆ.—Although numerous complications and sequelæ may occur in typhus fever, it is necessary to refer to but a few of them. Of these bronchitis stands at the head. This is so constant and prominent that it may be regarded rather as a symptom than a complication. It may generally be expected to occur. Among those complications which are infrequent may be mentioned lobar pneumonia, laryngitis, general convulsions, pyæmia, phlegmasia dolens, thrombosis, embolism, meningitis, and intestinal hemorrhage. General convulsions which are uræmic in origin constitute an exceedingly dangerous complication; they occur late in the disease, during the latter part of the second week. The attack is generally preceded by a greatly diminished amount of urine, at times amounting to suppression. The mental condition is also notably affected at this time, the stupor or delirium being intensified. The convulsions are usually followed by coma and death, the latter occurring within twenty-four hours.

DIAGNOSIS.—Typhoid fever is frequently mistaken for typhus, even by those having wide experience. Some of the essential points to be borne in mind in deciding between these diseases are as follows: Typhus fever has a very short and rather abrupt period of invasion. It usually commences with a slight chill or chilly sensation and a rapid rise of temperature, pronounced headache, and pain in the back and limbs. On the third or fourth day, rarely after the fifth or sixth, the characteristic eruption appears. In typhoid fever there is notably a long period of incubation and invasion. The patient has been suffering for days with general malaise (which is frequently regarded as due to malaria or general debility), and it is only after ten or fifteen days, when the symptoms have gradually become more pronounced, that he is obliged to go to bed and remain there. I regard this as one of the most important points in the differential diagnosis, and it can almost always be relied upon. This cannot be said of the diarrhœa and epistaxis, which are erroneously believed by some to be present in all cases of typhoid fever. When epistaxis is present it suggests at once typhoid fever. Murchison found it in but 12 out of 7000 cases of uncomplicated cases of typhus fever. Diarrhœa is likewise a very uncommon symptom of typhus fever, particularly before the crisis. Abdominal pain, tenderness, and tympanites, which are so constant in typhoid fever, are, as a rule, absent or only feebly marked in typhus. The characteristic eruptions of these diseases are markedly different. When typical, that of typhus appears on or before the fifth day and is found over the greater part of the body. When it is fully formed it is dusky in color, does not disappear on pressure, and there are no successive crops, as in typhoid. The eruption in this disease is not short lived, as in typhoid, but remains distinct for several days, and is usually present when death occurs in uncomplicated cases. In typhoid the eruption does not appear until the beginning of the second week. It is confined principally to the abdomen, back, and chest, and consists of small rose colored papules which disappear on pressure. Successive crops occur. It is in those cases in which the typhus eruption is slight or the typhoid eruption is profuse that errors are apt to occur. I cannot speak too strongly on this point. Numerous cases of typhoid have come under my observation which have been positively declared to be typhus fever on account of the accompanying general eruption. In some cases it was a profuse typhoid eruption; in others it was a septic eruption or an accidental one. It must be borne in mind that a profuse typhoid exanthem follows the ordinary course of the eruption in that disease; that is, in two or three days the first crop disappears and is succeeded by a second, or the first crop disappears and a much smaller crop follows. In other words, there are successive crops instead of a permanent eruption.

Accidental eruptions which sometimes accompany typhoid are, as a rule, short lived, and disappear on pressure or become indistinct in two or three days. A general eruption sometimes follows a high temperature. I have seen numerous cases where the history of the invasion and the early symptoms were clearly indicative of a typical case of typhoid fever; still, on account of a profuse eruption, either typhoid or foreign to the disease, the diagnosis of typhoid fever would not be accepted until corroborated by the autopsy. Even if the history of the eruption alone were carefully studied, it would, as a rule, help to clear up whatever doubt might exist as to the diagnosis. I wish to repeat that the early history of the case, particularly the period of invasion, should always be carefully taken into consideration before a decision is made.

In considering the differential diagnosis between measles and typhus fever, it should be remembered that measles is essentially a disease of children, while typhus affects adult life. The high temperature and pulse and early acute catarrhal symptoms affecting the eyes as well as the respiratory tract point toward measles. The bronchial or catarrhal symptoms accompanying typhus are not as acute or as early. The eruption of measles, although it may in a way be confounded with the early eruption of typhus, is particularly prominent on the face, where the eruption of typhus is absent. If measles occurs in an adult, the mental dulness and subsequent delirium which are marked in typhus are wanting. Special care should be taken to ascertain if there have been other cases of measles in the family or vicinity. It is well to remember that the eruption of two distinct diseases may be present at the same time. I have the notes of a well marked case of typhoid fever in the beginning of the second week which I saw in consultation at the New York Hospital in 1893. The typical eruption of typhoid fever was present on the abdomen. At this stage the temperature suddenly became higher and pronounced coryza and other catarrhal symptoms appeared. In two or three days the characteristic eruption of measles appeared on the face and chest. An investigation disclosed the fact that the patient, a young man, had attended his sister's children who were suffering from measles, shortly before he was removed to the hospital.

If the patient is closely observed and the present and previous history is carefully studied, malarial fevers can hardly be confounded with typhus. The periodicity which is usually prominent in malarial fevers, the controlling effect of quinine and other remedies, the history of the patient being at the time present in a malarial district or having previously lived in one, the absence of an eruption, the evidence of an enlarged firm spleen, etc., should exclude typhus fever.

A differential diagnosis between cerebral meningitis and typhus fever is not always easy at first. As a rule, however, in meningitis the cerebral symptoms occur earlier and are more marked, the headache is more intense, and the hearing is abnormally acute; there are also present photophobia and acute delirium. In meningitis symptoms of irritation or compression are very early noticeable, such as vomiting, ptosis, strabismus, unequal or contracted pupils, muscular rigidity, tremor or paralysis, etc., which are uncommon in typhus. Vomiting, which is a very common and constant symptom in meningitis, is very rarely seen in uncomplicated cases of typhus fever. Of course the presence of a well marked typhus eruption would decide between the diseases referred to. This, however, may not appear for two or three days.

Epidemic cerebro-spinal meningitis may be mistaken for typhus fever, but only in exceptional cases. Although the invasion of typhus is rapid, that of cerebro-spinal meningitis is markedly abrupt, and almost always occurs during the night with really no premonitory stage. Cerebro-spinal meningitis usually affects children before the tenth year, while typhus is a disease of adult life. In the latter the critical period occurs late in the disease. In cerebro-spinal meningitis death may take place within twenty four or forty eight hours, and the cerebral symptoms, such as intense headache, photophobia, phonophobia, and delirium, become at once prominent. In this disease, also, vomiting is almost always present, while it is rare in typhus. In cerebro-spinal meningitis the pain is marked over the nape of the neck and down the back over the region of the spine. On the third or fourth day contractions of the muscles of the neck and back are present. Retraction of the head and opisthotonos are more or less pronounced. The retraction of the head is a sign which is generally understood by the family, and constitutes a very important point in the diagnosis. The symptoms just referred to belong to cerebro-spinal meningitis, and are not found in typhus fever. An herpetic eruption is very commonly found about the lips, ears, and cheeks in cerebro-spinal meningitis, and only occasionally presents itself in typhus. The eruption of cerebro-spinal meningitis is irregular, has no definite form, and does not by any means always appear. It is usually found in certain parts where the temperature is supposed to be reduced, and is not spread uniformly over the body, as in typhus. I can hardly believe that a case of cerebro-spinal meningitis could exist where the diagnosis could not be made if the history and symptoms were carefully studied without the question of the eruption being taken into consideration, particularly after the lapse of two or three days.

Pneumonia is sometimes mistaken for typhus fever, and *vice versâ*. However, a thorough physical examination of the chest, with a careful investigation as to the history of the case, ought after a day or so to clear up whatever doubt may exist. Acute yellow atrophy of the liver and malignant endocarditis have also been mistaken for typhus fever.

PROGNOSIS.—Among the more important signs and symptoms which indicate an unfavorable prognosis are—advanced age, intemperate habits, a pulse in an adult of over 120, marked and persistent nervous symptoms, such as delirium, a dark and abundant eruption, great mental depression, disease of the kidneys or other organs, rapid respiration, insomnia which cannot be relieved. Uræmic convulsions and pronounced coma vigil almost always indicate a fatal termination. A pinhole pupil is also regarded as an extremely unfavorable sign; early relaxation of the sphincters, continued high temperature, particularly in adults, and also the advent of the different complications, tend to make an unfavorable diagnosis. It must be remembered, however, that although some of the signs above enumerated are almost invariably followed by a fatal termination, recoveries have taken place after their appearance; and every effort should be made to sustain life as long as possible.

PROPHYLAXIS.—Well directed and practical efforts toward the prevention of typhus fever in a community are far more important than the treatment of this disease; this fact, unfortunately, is too often overlooked. It can confidently be said that if the proper preventive means are employed an outbreak of typhus will soon be under control. It is of the utmost importance that cases of typhus fever should be early recognized, and that suspected cases should receive the most careful attention and care until they are proven not to be typhus. If in a private residence or small house, the patient should be placed in a well ventilated room on the top floor, everything in the apartment having been previously removed which is not absolutely needed for the patient, particularly upholstered articles. After removal, the clothing, bedding, etc. and the room previously occupied by the patient should be submitted to a rigid disinfection, as will be hereafter described. No one should enter the infected room except the nurses and physicians. This regulation should be particularly enforced, and food should be carried to the floor by an attendant and taken to the room by the nurse. The dishes should be placed in boiling water or a solution of bichloride of mercury, 1 : 2000, before being returned. Nurses leaving the apartment should remove all the clothing worn in the infected chamber before going outside, should have a bath and have the hair thoroughly washed; all linen, etc. when soiled should be put in tubs of boiling water, and afterward placed in a solution of bichloride of mercury, 1 : 2000. Worthless articles should be destroyed at once, preferably by burning. When the patient is able to leave the room he should be carefully and thoroughly bathed, rubbed, and dressed in fresh clean clothes, and removed to another room. The windows, doors, and all openings into the infected apartment should be sealed by pasting with strips of paper. The apartment should then be disinfected by sulphur dioxide, at least four pounds of sulphur to each 1000 cubic feet of air space; at the same time the air of the room should be rendered moist. The doors and windows and other openings should be kept closed for at least eight or ten hours, and longer if possible.

The most effective means of all for disinfection is heat. If a disinfection apparatus where a high degree of heat can be secured, such as is used by the Health Departments of different cities, is available, the clothing, mattresses, pillows, comfortables, and other material of this character which have already been subjected to the above fumigation and which cannot be washed, should by all means be heated in this manner or otherwise should be burned. Sulphur dioxide cannot be depended upon as a safe disinfectant in this instance, as it has very little penetrative power, and is only effective where bare surfaces are exposed. After fumigation the woodwork and wooden parts of furniture, beds, etc. should be carefully wiped with a solution of bichloride of mercury, 1 : 2000. I have referred above to a case occurring in a private residence. Cases originating in tenement or apartment houses and hotels should always be removed to a hospital or place prepared for the reception of such cases. Neither should cases of typhus fever be cared for in institutions unless a separate or distinct building be assigned for this purpose under the care of those who have absolutely nothing to do with the main building.

The admission of plenty of fresh air to the apartment greatly diminishes the danger of infection. Fresh air not only dilutes and greatly lessens the amount of infection, but is a very effective germicide, and is of inestimable value to the patient. As a matter of precaution in examining the body of typhus patients the bedclothing or clothing of the patient should be removed beforehand in order that the infected stratum of air be displaced.

I know of no circumstance which so strikingly illustrates the value of proper disinfection as a preventive agent as that which followed the disinfection of the infected Bowery lodging houses in New York City during the summer of 1893. It was found after a careful and extended investigation that the sources of infection in the cases of typhus fever received at the Reception Hospital during the spring of 1893 were almost all traceable to the lodging houses above referred to, about thirty in number, consisting of large four- or five-story buildings accommodating from fifty to two hundred lodgers. The Health Department at once ordered the thorough disinfection of these places. The walls, ceilings, floors, bedsteads, chairs, etc. were washed with a solution of bichloride of mercury, 1 : 1000, and then, while the walls and contents were still wet, each room was fumigated with sulphur dioxide. A large number of the mattresses which were old and worn out were destroyed. The others with the bedding were removed to the disinfecting plant of the Health Department and disinfected by heat. As a result of this procedure the number of cases of typhus fever occurring in New York was rapidly reduced. The following table will be more eloquent than words :

1893.	Number of cases of typhus fever removed to Reception Hospital.
First quarter (January, February, and March)	210
Second quarter (April, May, and June)	116
Third quarter (July, August, and September)	12

It may be added that the 12 cases occurring in the third quarter were received at the hospital during the early part of July. There have been no reported cases of typhus fever in New York City since the period referred to above, July, 1893.

TREATMENT.—Little can be said in the way of therapeutics. There is no specific for the treatment of typhus fever. The most rational and successful line of treatment consists in combating the different symptoms as they appear by proper nourishment, the judicious use of stimulants, agents which reduce the temperature, and narcotics and anodynes to allay pain and restlessness and produce sleep. Pure milk constitutes the most effective means of administering nourishment. If in its natural state it disagrees with the patient, Vichy or lime-water may be added or it may be peptonized. I cannot leave the subject of food without speaking strongly in favor of kumyss as a nourishing agent, for not only in typhus, but in all continued fevers, I know of no form of nourishment that equals this when it is properly made and administered.

It is made in this country from cow's milk fermented with yeast in tightly closed bottles. The coagulation which follows is essentially the same as that which is found in the stomach. The breaking up of this coagulum in the stomach requires considerable effort on the part of the muscular walls of this organ, which is frequently incapable of properly performing the task, and the milk is ejected. This commonly takes place in weak and badly nourished children and in those suffering from almost any severe form of disease. The coagulated milk constituting kumyss is shaken from time to time by the maker until it becomes fluid and is then ready for use. It will thus be seen that kumyss is milk practically ready for assimilation when it reaches the stomach. The carbonic acid contained in this beverage is usually very grateful to the patient, but if this gas is contraindicated the bottle may be left uncorked for a short time in the refrigerator. Kumyss also contains 2 or 3 per cent. of alcohol, resulting from fermentation, which is of great value in typhus fever. The acidity is also generally acceptable to the patient. The value of kumyss is frequently impaired by age, hot weather, etc.; it then becomes very acid and disagreeable, and perhaps irritates the stomach. My experience with beef extract in fever is unsatisfactory. There are numerous other forms of nourishment which have more or less value according to the experience of different physicians.

Cold baths and cold sponging are the agents which have been mainly depended upon at Riverside Hospital for the reduction of the temperature. This method appears to be universally endorsed by those who have had large experience in the treatment of this disease, particularly by Combemale, Petruso, and others. Petruso employed cold baths in two epidemics with very satisfactory results. The wet pack has been employed by some, and sponging may be used instead of the bath when deemed advisable. An objection to the plunge bath as ordinarily used is the necessity for transferring the patient to a tub, which requires some exertion on his part. This can be avoided by improvising a tub in the bed in the following manner: A large rubber sheet is passed underneath the patient, the upper end of which is carried over the pillow; on the sides and foot of the bed are placed tightly rolled blankets, the sides and lower end of the rubber sheet, already placed in position, are carried up and over the rolled blankets, making a receptacle in which the patient lies; water of the temperature of about 85° F. is now poured into the bath, and the temperature is further reduced to 75° F. by the addition of cold water or ice. The patient should be well rubbed while in the bath and carefully watched. As a rule, patients can remain in a bath of this temperature for fifteen minutes. The rolled blanket at the lower end or side can now be partly removed, and the rubber blanket so arranged that the contents of the tub can flow into a receptacle on the floor. The patient should now be thoroughly dried and rubbed and the rubber blanket removed. He should be carefully covered up and a stimulant administered. The cold plunge or bed bath is almost always followed by a marked reduction in the temperature; the pulse becomes stronger, a diminution in the delirium and restlessness takes place, and sleep often follows. The frequency with which these baths may be employed depends of course on the temperature; if this remains above

102° F., the baths are particularly indicated and should be used every three hours.

Quinine may be employed as an antipyretic when the temperature is high and the bath is contraindicated; it is at least a safe remedy. This, however, cannot be said of antipyrine, phenacetin, and remedies of this class. While they reduce the temperature, they are apt to cause considerable depression, which should be avoided. I believe this to be the feeling of the majority of those who have had experience in the treatment of typhus fever.

Stimulants are particularly indicated in this disease; their value is conspicuously apparent in the later stage, particularly in alcoholic subjects. Digitalis is used as a heart tonic and diuretic. Nitroglycerin and strychnine particularly may be also recommended as heart stimulants. Morphine, although objected to by some, is unquestionably valuable in the insomnia accompanying the disease when judiciously administered, and in comparatively small doses is certainly a cardiac stimulant. Innumerable remedies, such as sulphonal, trional, bromide, chloral, etc., have been used to relieve the insomnia with varying success, and may be given a trial. The fluid extract of guarana was a favorite remedy at Riverside Hospital, New York, during the epidemic of 1881-82 for the headache which is present in typhus fever. It is strongly recommended by Dr. Frank Chapin, who was in charge of the above hospital during the epidemic above referred to. One or two drachms of the fluid extract should be occasionally given. Sinakoski says that for over two years he treated typhus by every known method, and as a result he feels satisfied that the calomel treatment is superior to all others, and if begun early greatly diminishes the severity or aborts the disease. I cannot but feel that this writer is over confident regarding this form of treatment. I certainly do not believe that the disease can be aborted. Mr. H. T. Webster regards *Echinacea angustifolia* as a valuable antizymotic, and reports that he has used it with success in typhus fever. Schleschumizen reports good results from the internal use of creolin in doses of $\frac{3}{4}$ grain in distilled water four or six times daily. Under this treatment the disease was more submissive and pursued a milder course with a lower temperature. Dr. Vance of Sonoma, California, recommends that leeches be applied to the temple in young and robust patients. It will thus be seen that innumerable remedies and plans of treatment have from time to time been suggested, but I believe the method which I have already recommended, of treating the different symptoms and complications as they present themselves, is the most practical and valuable.

RELAPSING FEVER.

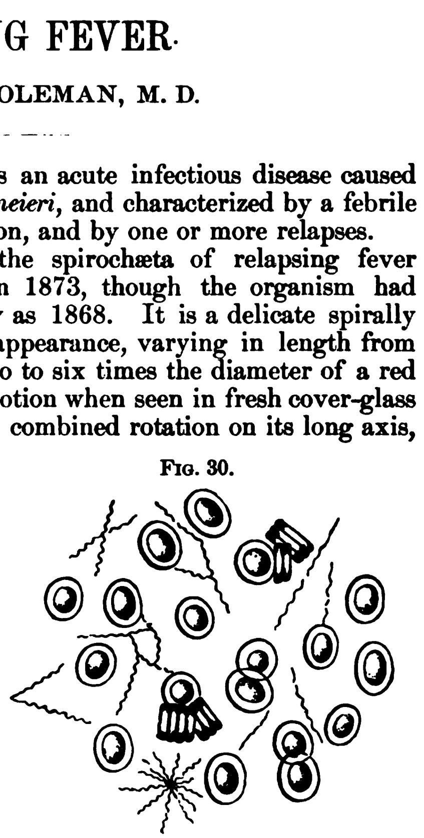
BY WARREN COLEMAN, M. D.

DEFINITION.—Relapsing fever is an acute infectious disease caused by a spirillum, the *Spirochæta Obermeieri,* and characterized by a febrile paroxysm, by a period of intermission, and by one or more relapses.

ETIOLOGY.—The discovery of the spirochæta of relapsing fever by Obermeier was made known in 1873, though the organism had been seen by this observer as early as 1868. It is a delicate spirally twisted filament of homogeneous[1] appearance, varying in length from 16–40 μ, or, approximately, from two to six times the diameter of a red blood cell, and is always in active motion when seen in fresh cover-glass preparations. Its movements are a combined rotation on its long axis, propelling the organism backward and forward, and a shortening or lengthening of its spirals, a portion of the organism straightening out at times and thrashing around among the corpuscles in whip-like fashion.

The spirochæta should be examined in an ordinary cover-glass preparation of blood and without the addition of any reagents, since it is extremely sensitive to them. Von Jaksch states that the mere addition of distilled water causes the organisms to disappear. Ordinarily they may be easily detected through the disturbance they create among the red blood cells. They occur singly or in groups, and may be seen with a $\frac{1}{6}$ inch (Leitz) objective, though it is desirable to use a $\frac{1}{12}$ inch homogeneous oil immersion lens and Abbe's condenser.

FIG. 30.



Blood of relapsing fever, showing Spirochæta Obermeieri among the red corpuscles; magnified 1150 times (Eichhorst).

The spirochætæ are found in the blood only during a paroxysm of fever, and disappear shortly before the end of the paroxysm. As a rule, they do not appear during the first two or three days after the onset of the disease. They may be present in great numbers in each field of the microscope, or there may be difficulty in finding a single organism. What becomes of the organisms during the period of intermission has not been determined.

The small number of cases in which absence of the spirochætæ from the blood has been reported may be disregarded in the face of the overwhelmingly positive results in the majority of cases. It is a notable fact that the number of spirochætæ varies at different times in the same individual during the same paroxysm, and Heydenreich, who made a careful study of the blood during an epidemic in St. Petersburg, set forth the opinion that fresh broods of the organism were probably produced several times during a paroxysm. This opinion was based upon the finding of only a few spirochætæ in the blood of a patient at one examination, yet a specimen taken a few hours later revealed their presence in large numbers. The same observer established a further interesting fact, that the spirochætæ after removal from the body survived but a short time at the body temperature, though if kept at a temperature from 60° to 70° F. they remained alive much longer. This would seem to show that the very pyrexia produced by the organism is in the end the means by which the paroxysm is brought to a close. Sarnow and v. Jaksch have observed in the blood between the paroxysms highly refractive bodies resembling diplococci, which they suggest may be spores. V. Jaksch states that at times he has seen these coccus-like bodies grow out into short rods.

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[1] A beaded appearance of the protoplasm has been noted by one or two observers.

Nothing is known of the habitat or life history of the spirochætæ, and up to the present time all attempts at artificial cultivation have failed.

A review of the epidemics which have occurred since Rutty described relapsing fever in 1770 leads to the conclusion that there are certain endemic centres (*e. g.* Ireland), and that when epidemics occur in other places infection has been carried to them by persons or fomites. The formerly-considered autochthonous origin of relapsing fever is evidence that the disease is at first endemic. All authorities are agreed that relapsing fever is communicable by personal contact, and the more intimate the contact the greater the likelihood of infection. Thus in crowded tenements the disease spreads rapidly; nurses and orderlies are more likely to contract it than hospital internes, and the internes than the attending physicians. When a person sleeps in a bed not yet cleansed which has been occupied by a relapsing fever patient, infection almost certainly follows.

As regards the transmission of relapsing fever by fomites, there seems to be some difference of opinion. Wyss and Bock, Cormack and Parry, have recorded instances where the disease was thus conveyed, while Loomis, on the other hand, states that in the epidemic in New York City in 1870 he found no evidence that the fever was conveyed by clothing, and that not a single person who was brought into immediate contact with the clothing contracted the disease.

It was thought formerly that relapsing fever originated in destitution and filth, hence the names "famine fever" and "hunger-pest," but it is known now that these exert simply a predisposing influence.

There has been much discussion as to the manner in which relapsing fever is transmitted from person to person. The expired air and the exhalations from the skin both have been accounted responsible for the spread of the disease. But we know nothing as yet concerning the channel through which the organism leaves the body or the form in which it leaves it, and until these facts can be ascertained opinion must be held in abeyance. The spirochæta is not present in the bronchial secretion, in the conjunctival secretion, or in the serum of the herpetic or sudaminal vesicles which occur in certain cases, and is found in the urine and matters vomited only when they contain blood. Heydenreich states that it does not leave the body in the fæces.

We are equally in doubt as to the manner in which the spirochæta effects entrance into the body. It has been thought that it passed in with the inspired air. But such a theory presupposes the formation of spores and their drying outside of the body, and appears to be contradicted by the readiness with which the disease is transmitted. From studies during the Breslau epidemic Litten concluded that the spirochætæ were not contained in the drinking water, and the organisms found by Carter in water from a tank in Bombay, though similar in form, were larger than those seen in the blood of relapsing fever patients. A manner of infection which has not received attention, and which seems upon *a priori* grounds not unlikely, is the introduction of the organism or its spores into the mouth by unclean fingers. The rapid dissemination of the disease in filthy, overcrowded apartments lends weight to this supposition. But, whatever may be the channel of infection, the important fact remains that relapsing fever is directly communicable from person to person.

Motschutkoffsky has shown that relapsing fever may be reproduced in man by inoculation with the blood of a patient ill with the disease, and several instances are recorded where infection followed wounding the hands at autopsies. Koch and Carter have produced relapsing fever experimentally in monkeys by inoculation.

Relapsing fever may occur at any age, though the greater number of cases have been met with between the ages of fifteen and twenty-five.

Neither sex nor season has any influence upon the development of the disease. That more males are attacked than females may be accounted for by the fact that males constitute by far the greater proportion of tramps and vagrants. One attack does not afford immunity against the disease.

PATHOLOGICAL ANATOMY.—The pathological changes caused by relapsing fever are in the main those of acute infectious diseases generally.

The *spleen* is enlarged during the active periods of the disease, sometimes enormously, and is dark and soft. Not infrequently it is the seat of anæmic infarctions and focal necrosis. According to Nikiforoff (Ziegler), microscopic examination reveals extensive degeneration of the pulp cells, amounting in places to actual necrosis, and the formation of fibrin in the veins of the pulp. The spirochætæ are found in considerable numbers in the areas which are not entirely necrotic. Hyperplasia of the spleen pulp occurs in other places. Abscesses occasionally form, and may give rise to peritonitis. Rupture of the spleen has occurred in some cases, followed by rapidly fatal syncope.

The *kidneys* are swollen, especially their cortical portion, lighter in color than normal from a granulo-fatty change in the epithelial cells, and streaked with the red, congested bloodvessels. Not infrequently the cut surface shows minute hemorrhages into the kidney substance.

The *heart muscle* undergoes parenchymatous degeneration. The fibres lose their striation and their nuclei may show fragmentation.

The *liver* is enlarged and congested, and its cells present parenchymatous changes.

The *stomach* and *intestines* may present a moderate grade of inflammation, as evidenced by injection of their vessels and minute extravasations of blood in their mucous membranes.

The *lymph nodes* are often infiltrated and swollen, but are rarely ulcerated.

SYMPTOMS.—*Incubation.*—The period of incubation in relapsing fever varies. Cases have been recorded in which the disease apparently followed within a day or two of exposure (Murchison), and others where the symptoms did not present themselves for twelve or fourteen days. The average period of incubation appears to be five to seven days. After experimental inoculation of apes with the blood of relapsing fever patients the disease does not appear until several days have elapsed, and in the case of experimental inoculation in the human subject by Motschutkoffsky symptoms did not follow for seven days.

Prodromata.—Relapsing fever is rarely preceded by prodromal symptoms. If they occur, they last only a day or two, during which time the patient suffers from anorexia, lassitude, slight headache, or vertigo. Generally, the disease is ushered in abruptly by rigors or a chill of moderate severity.

Invasion.—The attack usually begins during the day. Patients often can tell the exact hour of invasion, and not infrequently are seized while at work. Following the chill, there is a rapid rise of temperature, the thermometer registering 104° to 106° F. by the evening of the first or second day. In many cases there is a rise of 2° F. or more during the chill. Hyperpyrexia in relapsing fever, however, is not dangerous. Accompanying the rise in temperature, the pulse speedily becomes accelerated, reaching 110, 120, or even a greater frequency. It is full and strong at first, and in the average case continues good throughout the paroxysm, but may become feeble, compressible, and even dicrotic.

Early in the disease the patient suffers from extreme giddiness, so that he is unable to walk or even stand, and often takes to his bed from this cause. Headache of a most intense nature soon appears, and distressing pains occur in the muscles of the trunk and extremities, especially severe in the calves of the legs. The severity of the pains sometimes increases as the paroxysm progresses. Muscular hyperæsthesia, particularly marked over the gastrocnemii, adds to the suffering of the patient. Cutaneous hyperæsthesia may be present, especially in women. Pains occur also in and about the joints, though, as a rule, the joints are not swollen. Patients sometimes come into the hospital under the impression that they are suffering from acute articular rheumatism.

Nausea and vomiting usher in a certain proportion of cases. At first the contents of the stomach are expelled, and later mucus and regurgitated bile.

The face is flushed, but not dusky. The tongue is moist and coated with a whitish fur. Thirst is intense. There may be anorexia or the appetite may be increased. The skin becomes slightly jaundiced during the first few days, and in certain cases the color deepens. The jaundice is thought to be due to catarrh of the bile ducts. The bowels may be free or constipated. There is tenderness in the hypochondriac regions, and upon percussion the liver is found enlarged. The spleen increases rapidly and markedly in size, extending well below the free border of the ribs. It increases in size so rapidly that the enlargement may be noted from morning to evening of the same day.

A petechial eruption occurs in about 10 per cent. of the cases (Murchison). Herpes labialis and sudaminal vesicles are met with in some cases.

The urine presents the characters common to febrile conditions. It is diminished in amount, of dark color, and of higher specific gravity than normal, and it not infrequently contains albumin. Blood may be present. When the jaundice is marked the urine contains bile pigment.

The headache often diminishes, but the pains continue, sometimes with increasing severity as the disease advances. The suffering occasioned by moving causes the patients to lie perfectly still, but they are not apathetic. They are sleepless, but only because of the pains. Cerebral symptoms are not marked even when there is hyperpyrexia. Occasionally, however, there is delirium. The temperature remains at about the height it reached on the first or second day, with a diurnal variation of 2° F. or more. The time at which the remission occurs varies in different individuals. The pulse retains its frequency or is increased somewhat.

Crisis.—When these symptoms have continued about a week, and with apparently alarming severity, the crisis comes. It may occur as early as the fifth or be delayed until the fourteenth day. There is a sudden fall of temperature ordinarily of from 5.4° to 10.8° F. (Lebert) to the normal or below it. There is no disease in which the temperature falls so suddenly. Lebert has recorded a case in which the fall amounted to 12.6° F., and Murchison another in which it amounted to 14.4° F. in twelve hours. The pulse rate diminishes correspondingly, dropping from 120 to 70. Occasionally it falls as low as 52 or 48 (Lebert). The headache and pains disappear, the tongue becomes clean, and the patient passes into a fairly comfortable state. The crisis occurs most frequently in the night or early morning. On the evening of the last day of the paroxysm the temperature may rise suddenly as much as 4° F. Profuse sweating, diarrhœa, epistaxis, or the menstrual flow not infrequently occurs at the crisis, or the patient may become wildly delirious immediately before the crisis, and be perfectly rational after it has passed. As a rule, the pulse continues a little above the normal, and is especially likely to be accelerated if the patient attempts to get out of bed, but the appetite returns and he improves rapidly, feeling perfectly well in a short time. If he is in an hospital, he may insist upon returning to work. But his apparent recovery is of short duration.

Relapse.—A relapse is sure to follow except in a limited number of cases. It usually occurs on the seventh day and at night. It may occur earlier, even as early as the second or third day. The symptoms return with all their severity. The temperature rises to about the height it attained during the first paroxysm, the pulse becomes accelerated, and again the patient suffers from the headache and muscular pains. The duration of the relapse is variable, the average being from three to five days, after which a second crisis comes.

At times when the first paroxysm is mild in character the relapse is severe, and *vice versâ*. In the majority of cases convalescence is established after the relapse, but two, three, or even more relapses may occur.

Sudden collapse, occurring without any apparent cause, is a dangerous and usually fatal symptom in a limited number of cases. The attack may have been mild and have been progressing favorably, when suddenly symptoms of cardiac failure come on. These may occur at any period of the disease, but are most likely to manifest themselves at the first or second crisis. The pulse becomes small, rapid, and feeble, the skin is bathed in a cold clammy sweat, and the patient passes into a state of unconsciousness, to be rapidly followed by death. In some cases the pulse gives evidence of the impending cardiac failure a day or so before the crisis, but in others there may be no indication of the danger until it arrives. Murchison found the heart fatty and dilated in three cases where it was examined post-mortem. In other cases a sudden effort, such as getting out of bed, induces cardiac failure.

Occasionally there is a *pseudo-crisis* toward the end of the first paroxysm. The temperature falls suddenly, perhaps below the normal, and the distressing symptoms abate. But about twenty-four hours afterward the temperature rises to 104° F., the headache and the pains return, and the actual crisis is delayed for twenty-four or forty-eight hours longer. According to Carter, the blood during these attacks shows the presence of the spirochætæ.

DURATION.—The average duration of relapsing fever is from eighteen to twenty days. After an attack patients regain their health slowly. Convalescence is long and tedious. Even when the disease ends with a single relapse it is often six weeks before patients can resume work, whereas if they have more than one relapse the return to health is much longer delayed.

Abortive cases occur in relapsing fever as in many other specific infectious diseases. Convalescence may be established after a light first paroxysm, or there may be a relapse of short duration. In either case patients recover their health quickly.

Griesinger introduced the term *bilious typhoid* to include what he considered a distinct type of fever attended by jaundice and by a typhoid condition. There is some doubt, however, as to what disease he was describing. Since there is a form of relapsing fever, proved to be such by the presence of the spirochætæ in the blood, and attended by jaundice and a continuance of the pyrexia between the paroxysms, Murchison concluded that all the cases described by Griesinger were of this nature. Equally eminent authorities, however, contend that bilious typhoid is the disease now known as acute infectious jaundice. (See Weil's Disease, page 945.)

COMPLICATIONS AND SEQUELÆ.—*Lobar pneumonia* is the most common of the serious complications of relapsing fever, though the frequency with which it occurs varies greatly in different epidemics. It develops, as a rule, during the paroxysm or the relapse, and is especially likely to involve both lungs. Persons of intemperate habits are most often affected. The cases may be mild or severe. Pulmonary gangrene follows the pneumonia in a small proportion of cases. In many epidemics this complication has increased the mortality rate perceptibly.

Bronchitis is perhaps the most frequent complication of relapsing fever. Generally it is mild in character.

Abscesses may form in the spleen and render convalescence slow and tedious, or may lead to a fatal termination through peritonitis or metastatic pyogenic processes in other parts of the body. *Rupture of the spleen*, without abscess formation, has occurred, accompanied by sudden and intense pain in the splenic region and followed by a rapidly fatal syncope.

Dysentery is a dangerous and oftentimes fatal complication in certain epidemics.

Meschede states that *purulent otitis* occurs in about 10 per cent. of the cases. One or both ears may be affected.

Parotiditis is rare. When it does occur the inflammation usually proceeds to suppuration and delays convalescence.

Epistaxis may be a dangerous complication.

Though the urine in relapsing fever not infrequently contains traces of albumin, symptoms of kidney disease rarely occur. When symptoms of uræmia do appear in the course of the disease, they usually depend upon a pre-existent nephritis.

Pregnant women always abort or have premature labor when attacked with relapsing fever. In the majority of instances the mother survives, but the child dies, even though viable when born.

Among the more important of the sequelæ of relapsing fever is a post-febrile *ophthalmia*, which occurs in two stages—an amaurotic and an inflammatory stage. The inflammation may involve the iris alone or the iris and choroid coat, and is accompanied by intense intraorbital pain. Optic neuritis occasionally occurs. As a rule, only one eye is affected. Loss of vision not infrequently follows. At times the headache and muscular pains persist after the paroxysms subside, and render convalescence long and tedious.

DIAGNOSIS.—Difficulty in recognizing relapsing fever can occur only during the first few days of the disease, and before the spirochætæ have appeared in the blood. In its mode of onset it is not unlike typhus fever, yellow fever, and smallpox. But with the exception of typhus fever, fully developed cases present little difficulty. Epidemics of relapsing fever and typhus fever have prevailed at the same time, and under these circumstances it may be impossible to decide which disease one has to deal with until positive evidence of the one or the other presents itself. There is the same absence of prodromal symptoms in both diseases, the same abruptness of invasion, the same rapid rise of temperature. In both diseases headache and muscular pains are prominent early symptoms. But in typhus fever prostration, in relapsing fever giddiness, compels the patient to seek his bed. In typhus fever the face is dusky—in relapsing fever, flushed. In typhus fever dulness of intellect accompanies the headache—in relapsing fever the mind remains clear. And by the third day, often earlier, the spirochætæ may be found in the blood in relapsing fever.

PROGNOSIS.—Relapsing fever is not a dangerous disease, despite the severity of its symptoms, and is not often a cause of death in itself. A fatal termination rarely occurs except from sudden collapse or some complication. The extreme limits of the mortality rate in the epidemics which have occurred are 2 and 11 per cent. The higher of these percentages has occurred when complications were frequent. Pneumonia is the complication to be most feared, with the exception of pyæmia following splenic abscesses and dysentery. Rupture of the spleen may be regarded as an accident, and needs scarcely be taken into consideration in forming a prognosis. Even though pneumonia occurs, the case may terminate favorably. Relapsing fever is more serious in chronic alcoholic subjects and in old people.

Cardiac thrombosis is stated to be a cause of death in some cases, especially in persons whose previous health has been bad or in those of intemperate habits. The cardiac thrombosis is probably, however, only a concomitant of death, the actual cause being a degenerated myocardium.

TREATMENT.—The treatment of relapsing fever is wholly expectant. The use of various drugs has been proposed with a view to abort or modify the course of the disease, but all alike have proved unsuccessful. We are powerless to do more than combat the symptoms as they arise. Quinine is of no avail.

The headache which is such a pronounced feature at the onset of the disease may be relieved or diminished in intensity by the application of an ice-bag to the head. If this fails, morphine should be employed in sufficient quantity to relieve the headache and enable the patient to sleep. For relief of the muscular pains Lebert recommends rubbing with a mixture of equal parts of oil and spirit of chloroform. The bowels should be moved at the commencement of the attack with a single dose of calomel and sodium bicarbonate, or with small doses of calomel repeated every half hour until a grain and a half or two grains have been given, and followed by a saline in the morning. Later in the disease hydragogue cathartics may be administered to keep the bowels open, but care should be taken not to push their action too far. If there is diarrhœa, it should be stopped by the use of opium, bismuth subnitrate, and astringents.

The diet should consist of nutritious and easily digested foods. Further than this, no special precautions need be taken in the majority of cases. Should the patient's appetite be voracious, there is no objection to gratifying it within reasonable limits. Patients who are badly nourished and ill fed should be placed upon a generous diet immediately.

Sponging the body with tepid or cold water or the use of the cold bath is the best means of controlling the temperature. Internal antipyretics are not to be recommended, because of their depressing action on the heart. If delirium is present, the bromides and chloral should be used to control it.

Symptoms of uræmia demand the active employment of measures to promote the excretion of urea. Murchison advises that one or two drachms of potassium nitrate, one drachm of dilute nitric acid, and half a drachm of the tincture of digitalis be taken in divided doses during the twenty-four hours. The infusion of digitalis, combined with potassium acetate, potassium citrate, or sweet spirits of nitre, will be useful for this purpose. Water should be taken freely, and copious perspiration should be induced by means of hot-air or vapor baths.

Hydragogue cathartics may be used to cause a vicarious excretion of urea by the intestines.

In old and otherwise debilitated subjects stimulation with alcohol should be commenced at the first indication of enfeebled heart action. Sudden collapse demands the free hypodermic use of stimulants, such as ether, nitroglycerin, strychnine, and camphorated oil (camphor 1 part, olive oil 8 parts).

During the intermission the patient must be watched for fear that some complication may develop. It may not be necessary to confine him to bed, but it is advisable that he should remain indoors. If complications arise, they must receive appropriate treatment.

Parotiditis should be treated with hot or cold applications, whichever is the more agreeable to the patient. As soon as suppuration is detected a free incision must be made, the pus evacuted, and the wound dressed antiseptically.

The treatment during convalescence may be summed up as follows: a generous diet, tonics, and a moderate amount of alcohol with meals. Bitter tonics before meals, ale, porter or port wine with meals, and iron after meals will hasten the recovery of the patient.

YELLOW FEVER.

BY GEORGE M. STERNBERG, M. D., LL.D.

DEFINITION.—Yellow fever is a specific infectious disease in which one attack, as a rule, protects from subsequent attacks. The febrile paroxysm inaugurating an attack usually lasts from two to five days, and is followed by a period of great depression of the vital powers, during which there is a tendency to suppression of urine and to passive hemorrhage from mucous membranes. The urine contains albumin, the skin has a more or less pronounced icteric hue, and in fatal cases "black vomit" is usually ejected before death.

ETIOLOGY.—Yellow fever is not a contagious disease in the strict sense of the word—*i. e.* it is not usually contracted by contact with the sick—but, as in cholera and in typhoid fever, the infectious element multiplies in the body of the sick, and epidemics usually extend from foci of infection originating from the introduction of cases of the disease into localities previously free from it. Although not definitely demonstrated, it seems extremely probable that this occurs in the same way as in the diseases mentioned—viz. through the excreta. This is indicated by the fact that while contact with the sick as nurse or physician does not lead to infection, the soiled clothing and bedding of yellow fever patients may induce an attack in those who handle them, and may originate an epidemic when transported, without having been disinfected, to another locality. When yellow fever prevails as an epidemic, physicians and nurses are very liable to contract the disease because they are necessarily exposed in the infected localities, not because they come in contact with sick. This is an important fact which is established by abundant evidence, and yet it is denied by many physicians living in cities where the disease is endemic, who insist that the disease is transmitted by personal contagion. This opinion no doubt arises from the mistaken assumption that successive cases in the same house or neighborhood are directly connected in their etiology one with another, as commonly occurs in the strictly contagious diseases—*e. g.* smallpox or measles. On the contrary, they all contract the disease from a common and external source—the infected locality. It is well known that certain local and climatic conditions are essential for the development of the infectious agent ("germ") outside of the human body, and the consequent establishment of an external focus of infection and the epidemic prevalence of the disease. On the contrary, we have numerous observations which show that the introduction of cases or of fomites into localities where conditions are not favorable for the external multiplication of the infectious agent does not result in the occurrence of other cases in the vicinity, as would follow if the disease was propagated by personal contact. This is well illustrated in the city of Mexico, and at Petropolis, a health resort in the mountains a few hours' journey from Rio de Janeiro. Yellow fever is endemic at the sea-coast city of Vera Cruz, and during the summer months persons from the interior who visit this infected locality are very likely to contract yellow fever. Persons coming from the city of Mexico for a short visit on business or pleasure frequently fall sick with the disease after their return to their homes, but they never communicate it to those associated with them, and no focus of infection is developed as a result of their presence in the crowded and rather dirty capital city, which is located at an elevation above that at which the infectious agent is able to propagate itself outside of the body of the sick. The same is true as regards Petropolis, which is a health resort during the epidemic season for unacclimated persons residing in Rio de Janeiro. Communication between the two places is unrestricted, and individuals exposed in Rio not infrequently fall sick in Petropolis, but they never communicate the disease to others. This is also the experience of physicians in charge of hospitals located in healthy suburbs of infected towns. So long as the hospital and its vicinity remain uninfected, cases do not originate in its wards as a result of the admission of yellow fever cases, although these may be cared for by susceptible attendants and treated in the same wards with patients suffering from other diseases.

"In his report upon the camps established near Memphis in the epidemics of 1878 and 1879, Colonel Cameron makes the following statement: 'It was found necessary that the officer in authority should set an example of constant indifference to attack in order to appease, as far as possible, the constant anxiety of the population under his charge. Especially was this true in 1878, as depopulation went on slowly that year, and infected people poured daily into the camps from the more pestilential portions of the city. Very many reached camp with the fever on them, so that as many as seventeen persons fell victims in one night, not a few in their tents. In no instance, however, did they communicate the disease to their families or bed-fellows, as far as could be traced.'

"In the same epidemic (1878), Dr. Minor reports that over thirty cases were discovered among refugees in Cincinnati, O., and says: 'No physician or nurse contracted the disease, and in no instance did it exhibit any tendency to spread.' The same was true in Nashville the same year; twenty imported cases occurred in different parts of the city without any local cases resulting from them. Evidence of this kind could be extended to fill a volume; but sufficient has been presented to establish the statement made, and the reader may be referred to the 'proofs of non-contagion' in the second volume of the classical work of La Roche (pp. 236–566.)"[1]

Formerly many of those who denied that yellow fever could be transmitted by personal contagion assumed that it could not be transmitted, and ascribed outbreaks to local insanitary conditions, together with the favorable meteorological conditions recognized as essential for the development of an epidemic. These believers in the "local origin" of the disease denied the necessity for isolation of the sick and quarantine restrictions, while the "contagionists" insisted upon the exotic origin of the disease and its transmissibility by ships, persons, and fomites. That this latter view is correct is beyond question, although, as we have shown, the disease is not usually communicated by personal contact, and favorable external conditions are as essential for the development of an epidemic as is the introduction of the specific infectious agent.

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[1] Quoted from the writer's article on Yellow Fever in Wood's *Reference Handbook of the Medical Sciences*, vol. viii. p. 55.

As heretofore suggested, the yellow fever patient, like the patient with cholera or typhoid fever, probably carries "germs" in his intestine which are capable of abundant development outside of the body when local conditions are favorable. As to the specific germ, we have no exact information, inasmuch as all attempts to demonstrate its presence in the bodies of the sick or to isolate it from the excreta have been unsuccessful. But the conditions favorable for its development are well established.

Yellow fever is endemic at certain places upon the sea-coast of North and South America and the islands in the Gulf of Mexico, and from these places it is disseminated by human intercourse. Epidemics commonly develop as a result of the arrival from an infected locality of an individual who has been taken sick *en route* or after his arrival. But they may originate from the introduction of infected articles, independently of any imported case. The origin of several epidemics has been traced, with great probability, to the unloading of earth ballast from the vicinity of an infected city upon the wharves of a healthy seaport during the season favorable for the development of the disease.

As a rule, some time elapses after the introduction of a case or of "fomites" before the outbreak of a local epidemic. This interval varies according as local conditions are favorable or otherwise for the development of the infectious agent.

Yellow fever is essentially *a disease of the sea-coast*, and especially of large cities in an unsanitary condition, but when circumstances are favorable it may extend into the interior, following routes of travel, and especially navigable rivers.

It is, however, confined to the lower levels even in tropical or subtropical regions. In the Antilles the disease rarely prevails at an altitude above 700 feet. In Mexico the cities of Orizaba, Jalapa, and Puebla, which are more than 3000 feet above the sea level, have never suffered from the disease, although they have unrestricted communication with the infected seaport, Vera Cruz. In Spain, where several severe epidemics have occurred, the disease has rarely prevailed at an altitude above 1000 feet. The epidemic at Madrid (altitude 2000 feet), which occurred in 1878, was, however, an exception to this rule. In the United States a severe epidemic occurred at Chattanooga, Tenn., in 1878. This town has an altitude of 745 feet, which is the highest point at which the disease has prevailed in this country.

Temperature is an essential factor in determining the prevalence of yellow fever in those places where it is endemic and in the establishing of new centres of infection. Although the disease prevails to some extent throughout the year in the cities of Havana, Vera Cruz, and

Rio de Janeiro, it is especially prevalent during the hot season in these cities, and its epidemic extension occurs only in the summer months. The seasonal prevalence in the city of Havana is shown in the following table, compiled by Chaillé:[1]

Mortality from Yellow Fever in the City of Havana for Ten Years, 1870 to 1879, inclusive (Chaillé).

Month.	1870.	1871.	1872.	1873.	1874.	1875.	1876.	1877.	1878.	1879.	Average of ten years.
January	6	18	20	32	7	16	24	8	26	11	17
February	4	23	13	23	4	16	24	9	13	13	14
March	4	12	4	27	18	32	29	11	5	6	15
April	6	34	4	37	22	34	33	8	28	13	24
May	14	91	13	127	85	32	103	16	33	40	57
June	66	201	68	378	172	142	292	143	184	237	188
July	112	234	68	416	361	187	675	249	304	475	328
August	201	138	70	127	416	144	250	285	374	417	242
September	91	72	59	35	186	102	97	234	179	148	120
October	77	55	38	28	91	109	42	185	106	44	78
November	49	51	85	5	42	105	31	150	33	31	60
December	35	42	73	9	21	82	19	76	34	9	40
Total	665	991	515	1244	1425	1001	1619	1374	1559	1444	

In places which have a mean winter temperature below 65° F. the disease, when introduced, cannot establish itself as an endemic. The development of an epidemic requires a temperature of 75° to 80° F., maintained for some time, and upon the approach of cool weather the progress of the disease is checked. When the temperature falls below the freezing point it is usually completely arrested, and, as a rule, the disease does not recur during the succeeding summer unless it is again introduced. Epidemics may terminate before the occurrence of cold weather simply because all susceptible persons in the infected area have suffered an attack of the disease. Under these circumstances the continued activity of the morbific element ("germ") is shown when "unacclimated" persons venture to visit the infected locality; and many lives have been sacrificed by the premature return of refugees to their homes in the belief that they could safely do so, as no new cases had recently occurred in the pest-stricken town.

Atmospheric moisture and precipitation influence the development of yellow fever epidemics, and in arid, desert regions the disease is unknown. But while a certain amount of atmospheric humidity and soil moisture is essential, the disease has sometimes committed its greatest ravages during unusually dry seasons. Heavy rains by purifying the atmosphere and washing away accumulations of filth may exercise a favorable influence upon the progress of an epidemic. The *trade winds* of the tropics, and strong sea-breezes in general, are beneficial from a sanitary point of view, and places exposed to their continuous action rarely suffer from the disease under consideration. They dilute and carry away the poisonous emanations from insanitary places, and refresh and invigorate those who inhabit localities exposed to their action.

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[1] *Report to the National Board of Health*, Washington, 1880.

The wind has little to do with the dissemination of the disease. This is shown by the fact that vessels which anchor some distance from the shore in the vicinity of infected places do not suffer from the disease so long as they are kept in a good sanitary condition and unacclimatized members of the crew are not permitted to go on shore, while vessels lying at the wharves are very liable to become infected.

The board of experts appointed by Congress to investigate the epidemic of 1878 arrived at the following conclusion: "We know of no instance, either from our own observations or from the published records of yellow fever, in which it has been established that the disease has been carried to any considerable distance by atmospheric currents or by any modes or vehicles of conveyance other than those connected with human traffic and travel."

SANITARY CONDITIONS.—When the infectious agent is introduced by the sick or by means of fomites to localities in the "yellow fever zone" during the season favorable for the epidemic prevalence of the disease, its propagation without doubt depends largely upon local insanitary conditions, and it is doubtful whether it could effect a lodgement in a clean and well paved city. Its epidemic prevalence in New York and Philadelphia during the latter part of the last and the early part of the present century was during a period when these cities were for the most part unpaved, unsewered, and unclean. And it is in similar localities in the cities now most subject to invasion that it usually first appears and most persistently remains. In Havana, Rio de Janeiro, and other endemic foci of the disease it is especially prevalent in low-lying, filthy districts with unpaved streets. Organic matter of animal origin in a state of decomposition appears to afford a favorable nidus for the germ, and the accumulation of fecal matter in exposed situations is favorable to the development of an epidemic. Reasons have already been given for the view that the excreta of the sick contain the specific infectious agent. Dr. Parkes, the English hygienist, maintained the fecal origin of the disease. He says: "To use a convenient phrase, yellow fever, like cholera and typhoid fever, is a fecal disease. And here we find the explanation of its localization in the West India barracks in the olden time. Round every barrack there were cesspits, often open to sun and air. Every evacuation of healthy and sick men was thrown into, perhaps, the same places."

One method by which infectious material may be transported from such exposed filth-beds to the stomach of individuals living in the vicinity has recently attracted considerable attention in connection with the propagation of cholera. This is through the agency of flies, which may come directly from a cesspool to the kitchen or dining-room, and there contaminate articles used for food or drink. In this connection, however, it is well to call attention to the fact that the epidemic prevalence of the disease has never been shown to depend upon the use of a contaminated water supply, as is the case in cholera and typhoid fever. In cities having a common water supply the disease is not generally diffused at the outset of an epidemic, but it extends rather slowly from certain infected foci to which it has been introduced in the first instance or subsequently.

BACTERIOLOGY.—We have seen that the development of a yellow fever epidemic depends upon conditions external to the human body relating to temperature, filth accumulation, etc., and in the present state of science we are justified in the inference that the specific infectious agent which multiplies in presence of such conditions is a living micro-organism of some kind. But the morphological and biological characters of this hypothetical germ have not yet been demonstrated. This assertion is based upon the personal investigations of the writer made in Brazil, in Cuba, in Mexico, and in the United States in accordance with an act of Congress (1887) authorizing such an investigation. In my report[1] of these investigations I have formulated my conclusions as follows:

"The most approved bacteriological methods fail to demonstrate the constant presence of any particular micro-organism in the blood and tissues of yellow fever cadavers.

"The micro-organisms which are sometimes obtained in cultures from the blood and tissues" (immediately after death) "are present in comparatively small numbers, and the one most frequently found (Bacillus coli communis) is present in the intestine of healthy individuals; consequently its occasional presence cannot have any etiological import. . . . .

"Having failed to demonstrate the presence of a specific germ in the blood and tissues, it seems probable that it is to be found in the alimentary canal, as is the case in cholera. But the extended researches made, and recorded in the present report, show that the contents of the intestine of yellow fever cases contain a great variety of bacilli, and not a nearly pure culture of a single species, as is the case in recent and typical cases of cholera.

"Comparatively few liquefying bacilli are found in the fæces discharged during life or in the intestinal contents collected soon after death from yellow fever cadavers. . . . .

"Some of the micro-organisms present in the dejecta of yellow fever patients, as shown by stained smear preparations, have not developed in the cultures made, either aërobic or anaërobic. One extremely slender, filiform bacillus, which can only be seen with high powers, and which is quite abundant in some of my preparations, has never been obtained in the cultures made, and no doubt there are others in the same category.

"That the yellow fever germ is strictly anërobic, or that it will only grow in a special nidus, may be inferred from certain facts relating to the extension of epidemics."

It may eventually be found that the micro-organism which produces this disease belongs to an entirely different group from the bacteria: we are disposed to believe, however, that it is an anaërobic bacillus which multiplies in the intestines or in fecal accumulations outside the body, and which produces a deadly toxin (toxalbumin?) to which the phenomena of the disease are due.

In view of the facts heretofore recorded and the conclusions reached as a result of experimental investigations it is evident that the dejecta of yellow fever patients should be regarded as infectious material, and should never be thrown into privy vaults or upon the soil until they have been completely disinfected.

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[1] *Report on the Etiology and Prevention of Yellow Fever*, Government Printing Office, Washington, 1890.

Susceptibility and Immunity.—When yellow fever prevails as an epidemic all persons exposed within the infected area who have not previously suffered an attack are liable to contract the disease. But there is considerable difference in the susceptibility of individuals, and the negro race is generally believed to be less susceptible than the white. This is manifested, however, by the comparatively mild character of the attack rather than by an immunity from the disease. According to La Roche, the mortality among the whites on the island of Jamaica was 102 per 1000, and among the blacks 8 per 1000; in the Bahamas the mortality of the whites was 59 per 1000, that of the blacks 5.6 per 1000. In the great epidemic of 1878 the negroes appear to have furnished a considerable proportion of the cases, and in certain localities the mortality among them was considerable. Thus at Brownsville (Tenn.) 162 cases with 21 deaths occurred among the colored population; at Chattanooga, in a total of 685 cases, 429 were colored and 256 white, while the mortality among the blacks was 46 and among the whites, 118; at Decatur (Ala.) 64 cases and 28 deaths occurred among the whites, and 186 cases with 21 deaths among the blacks. The natives of northern latitudes are generally believed to be more susceptible than those born in tropical or subtropical countries, and the mortality among the fair-skinned natives of the North is higher than among natives of Southern Europe. Blair, as a result of observations made in Guiana, says: "The lower the winter temperature in the native country of those attacked, the more severe was their sickness; so that, while the mortality among West Indians amounted to only 6.9 per cent. of the sick, it rose to 17.1 among the Italians and French, 19.3 among the English, 20.2 among the Germans and Dutch, and 27.7 among the Scandinavians and Russians."

The mortality among the indigenous races of the West Indies and of those parts of North and South America in which the disease prevails occasionally or habitually, and of Mongolians living in these regions, is also less than among the whites; but none of these races have an immunity from attack.

A single attack of yellow fever usually protects from subsequent attacks, especially if the individual continues to reside in one of the endemic foci of the disease. While second attacks are comparatively rare, and some authors of experience have asserted in positive terms (Blair and others) that they never occur, there is ample evidence that one attack is not always protective. Thus, "Dr. Jackson states that in Spain, during the epidemic of 1820, 20 well authenticated instances came within his knowledge of persons being attacked who had had the disease before." Dr. Wragg, speaking of the epidemic in Charleston in 1854, says: "Six of these were so well proved as to admit of no doubt on the subject. Some of the patients were identified as having gone through the fever in this (the Roper) hospital in 1852, throwing up black vomit on both occasions" (La Roche). Dr. Rush also observed second attacks in Philadelphia in persons who had suffered a comparatively mild first attack.

In localities such as Havana and Rio de Janeiro, where yellow fever has established itself as an endemic disease, the adult native population enjoys an immunity which is almost absolute, and has been supposed to be hereditary. This view, until recently, was generally accepted by physicians residing in these endemic foci of the disease. There is, however, accumulating evidence that the immunity enjoyed by "creoles" is not inherited, but results from a mild and usually unrecognized attack during infancy or childhood. Dowler, writing of the epidemic of 1853 in New Orleans, says: "Many creole children had, during the epidemic of 1853, a fever, a slight fever—yellow fever, if you please, known as such rather by the coexistence of the epidemic than from any severe symptoms among these children—a slight fever never yet described, having generally but one paroxysm, lasting from six hours to one, two, or three days, scarcely ever requiring medication. That a few of these cases acquired an alarming violence, and even proved fatal, is most true, most deplorable."

Hinemann writes with reference to Vera Cruz: "Until lately the physicians and people of Vera Cruz supported with fanaticism the dogma that natives were absolutely exempt from yellow fever. But the fearful epidemics of recent years (1875, 1877, 1878) have worked a change, for so many native children and adults suffered that the truth could no longer be denied that these do not enjoy an absolute immunity."

In Cuba the dogma that creoles are exempt from yellow fever did not withstand the searching investigation made by the Havana yellow fever commission of 1879.

In the epidemic of 1887 at Key West the children of "acclimated" Cubans, natives of Havana, born since the arrival of their parents at Key West, showed the same susceptibility to the disease as other children. The recent investigations of Guiteras also give strong support to the view that the immunity of adult creoles results from an unrecognized attack occurring during childhood. Blair, speaking of the epidemic in British Guiana (1851–54), says: "Infancy was one of the most favoring causes of the action of the yellow fever poison. The constitution of the new-born or young white creole was highly susceptible. He or she was truly in the category of new-comers."

The great susceptibility of new-comers who without previous "acclimatization" are exposed during the prevalence of an epidemic is generally recognized in those places where the disease is endemic; and, on the other hand, persons who have resided for some time in an infected locality seem to acquire a certain degree of immunity independently of an attack of the disease. The fact that foreigners may remain for years in Havana, in Rio de Janeiro, and other endemic foci of the disease without suffering an attack is well established. But those who have escaped for several years are liable to be attacked during a season of unusual epidemic prevalence. The disease is, however, less fatal in such cases than among unacclimatized strangers.

Owing to the immunity acquired in childhood or by long residence in the infected area, yellow fever is a disease of minor importance among the native population in cities where it is endemic. This is shown by the following figures: In the city of Rio Janeiro, which has a population of 400,000, the mortality from some of the principal causes of death in the year 1886, an epidemic year so far as yellow fever is concerned, was—from tuberculosis, 2077; diseases of the circulatory apparatus, 1458; diseases of the cerebro-spinal system, 1345; diseases of the digestive apparatus, 1097; malarial diseases, 1086; *yellow fever*, 1015. In the same year (1886) more than twice as many deaths among the civil population of Havana resulted from tuberculosis as from yellow fever. That the immunity enjoyed by the population of the infected cities mentioned is not due to climate, *per se*, is shown by the fact that country people living in the same latitude readily contract yellow fever when they visit these cities during the epidemic season; also by the fact that when the disease was first introduced to Rio Janeiro in 1849 the native population gave no evidence of immunity, and for several years the mortality among them was considerable.

The susceptibility of males and females probably does not differ materially, although a larger mortality occurs among males, because they more frequently and often recklessly visit infected localities, and because of the intemperate habits of some of those who fall victims to the disease—*e. g.* sailors and soldiers. A recent debauch is generally recognized as a predisposing cause.

PATHOLOGICAL ANATOMY.—An inspection of the exterior of the body of an individual who has recently succumbed to yellow fever furnishes indications which should at once arouse suspicion as to the nature of the disease, especially in localities where it is known to prevail. The integument presents an icteric hue which differs from the saffron yellow color of jaundice and is due to blood pigment. It resembles the color which is seen to follow a bruise causing an effusion of blood into the tissues, and is less intense and less uniformly distributed than the yellow produced by bile pigments. Moreover the depending portions of the body, as a result of hypostatic congestion and pressure, have a deeper coloration and are more or less livid and mottled. That this appearance is due to pressure and position is shown by the fact that when the body is placed upon the side or abdomen soon after death, the most dependent part still shows this livid and marbled appearance. The face often has a livid and turgescent appearance, like that of a person recently drowned, or the face and hands may appear cyanosed. The lips or gums are often soiled with dark blood as a result of passive hemorrhage during the last hours of life, and a little stream of black fluid may frequently be seen trickling from the corners of the mouth or nostrils. This is the so-called "black vomit," which flows from the distended stomach or is forced out by an accumulation of gas in the intestine. Cadaveric rigidity is established soon after death. In the warm latitudes where the disease habitually prevails putrefactive decomposition quickly occurs, and unless the autopsy is made within a few hours after the fatal termination of a case, postmortem changes are likely to complicate the pathological appearances resulting from the disease.

The *blood* in yellow fever presents no changes which can be recognized by a microscopical examination during the progress of the case or immediately after death, but there is a certain degree of disorganization of the red corpuscles in severe and fatal cases, as is shown by the yellow color of the serum from the presence of free hæmoglobin. This may be observed in blood drawn as early as the third or fourth day, but is much more pronounced in that obtained from the large vessels and cavities of the heart after death. The serum obtained from blisters in advanced cases also has a yellow color. That this is not due to bile pigments is shown by the chemical researches of Cunisset and others. Blood drawn during life does not coagulate readily, or the coagulum is soft and loose, and the blood in the heart and large vessels after death is usually fluid and dark colored. The cavities of the right side of the heart may, however, contain soft coagula, and the right ventricle sometimes contains a more or less decolorized fibrinous clot. The "disorganized" and diffluent condition of the blood has been supposed by some to account for the passive hemorrhages which are so characteristic of the disease. But it is evident that if the capillaries and larger vessels were intact no escape of blood could occur as a result of its loss of coagulability. The hemorrhagic tendency is rather to be ascribed to changes in the walls of the small vessels and capillaries which weaken their resistance to pressure; and several competent observers agree that the walls of these vessels undergo a fatty degeneration.

Upon removing the calvarium the *brain* and its *meninges* are usually found to give evidence of congestion. The pons and medulla are especially hyperæmic. The surface of the brain often presents little hemorrhagic points and its substance is tinted yellow. There is usually some effusion into the ventricles and in the subarachnoid space, the fluid being of yellow color and sometimes turbid. Schmidt of New Orleans has described certain changes in the sympathetic ganglia to which he attaches importance. These consist in a disappearance of the nuclei from most of the ganglion cells, and in a "peculiar fatty lustre" which they presented, even in specimens mounted in balsam.

The *lungs* occasionally contain hemorrhagic infarctions, and are hyperæmic, otherwise they present no evidence of pathological change.

The *heart* has been described by some authors as soft and friable. I have not observed this, and no evidence of fatty degeneration was found in slides mounted by Guiteras (1879), whose autopsies were made very promptly after death. On the other hand, Schmidt and Riddel believe that the muscular fibres undergo a fatty degeneration. The *pericardium* frequently contains a considerable quantity of yellow serum.

Upon opening the cavity of the abdomen the most important and characteristic pathological appearances will be found. The *stomach* almost always contains a considerable quantity of a grumous black fluid similar to that commonly ejected during the last hours of life—"black vomit." There is no mystery as to the nature of the pigment in this black fluid. It is undoubtedly blood pigment more or less changed by the acid secretions of the stomach. The writer has repeatedly verified the presence of numerous decolorized blood corpuscles by microscopical examination. These are often massed together in little clumps, and brownish pigment granules are seen attached to these masses or in their vicinity. The pigment is not dissolved in the fluid, but is present in the form of granules which are insoluble in water; consequently, the spectroscope fails to demonstrate the presence of blood pigment. But when the black matter is dissolved in acidified alcohol a positive result may be obtained. Freire and others have imagined that this black pigment is a product of the vital activities of some micro-organism. But this view is entirely without scientific foundation. By adding some drops of hydrochloric acid to blood diluted with water a dark fluid is obtained which does not differ in appearance from the black vomit ejected by yellow fever patients (Dantes). The mucous membrane of the stomach shows patches of congestion, and occasionally small red spots resembling ecchymoses, which, according to Schmidt, consist of "an unbroken network of minute vessels congested with blood and identical with the network of large capillaries which surrounds the aperture of the gastric glands." The congested patches present no uniformity, the number and extent differing in different cases. Some authors have supposed that the most important pathological changes in yellow fever occur in the stomach, and that the disease is essentially an infectious gastritis. Crevaux thinks that the most important lesion consists in a fatty degeneration of the cells which line the gastric glands and of the capillaries of the mucous membrane. In specimens obtained at some of my own autopsies in Havana, placed in alcohol very soon after death, there is evidence of inflammation in a certain proportion of the cases. This is shown by the presence of collections of leucocytes in the submucous coat. But this appears to be rather exceptional than otherwise.

The *small intestine*, and especially the ileum, often contains a black fluid similar to that found in the stomach or, more frequently, a grumous, black material which consists of mucus and blood pigment and is smeared over the mucous coat of the gut. This usually comes from the stomach, but in some cases is due to a passive hemorrhage from the mucous membrane of the intestine itself, which is sometimes uniformly red as a result of hyperæmia or may present arborescent patches of congestion similar to those seen in the stomach. The large intestine occasionally shows a like appearance, but is usually normal.

The *liver* presents the most constant and characteristic pathological changes. As a rule, it is of a pale yellow or brownish yellow color, like that of new leather in its various shades, and contains comparatively little blood. But it is sometimes livid and gorged with blood, presenting a dark blue or purple color. This is especially apt to be the case when death occurs after a very brief illness—two or three days. As the victims of chronic alcoholism are especially apt to succumb to an attack of yellow fever, evidence of interstitial hepatitis is not infrequently found associated with the lesions characteristic of yellow fever. The dimensions of the liver, except in comparatively rare cases in which it is gorged with blood, do not differ materially from the normal. The parenchyma is more or less friable and easily torn, owing to the fatty change in the cells. On section the liver tissue is found to be drier than normal and to present the "boxwood" or "new leather" color characteristic of the disease, unless death has occurred during the stage of hyperæmia, which probably usually precedes that of anæmia and fatty degeneration. The cells are not uniformly changed, but areas of greater or less extent are seen in which they are infiltrated with fat globules. These are of varying dimensions, and one or several may be contained in a single cell. The nuclei often remain intact in these cells infiltrated with fat, but, according to Schmidt, "a great number of nuclei may also undergo fatty degeneration." Not infrequently the central vein is surrounded by normal cells, while those cells about the periphery of the lobule contain many fat globules.

In two of the livers brought back from Havana by the Yellow Fever Commission of 1879, in which there were evidence of cirrhosis, Woodward found that, in addition to the fatty change described, "an abundant infiltration of leucocytes was observed, not merely in the abnormally developed interlobular connective tissue, but also in the parenchyma of the lobules." I have also found a rather extensive infiltration of leucocytes in two cases, and in one of these a veritable necrosis of the cells had occurred in limited areas in the vicinity of the infiltration. Councilman, who made a careful study of material obtained at my autopsies in Havana (1888, 1889) discovered a form of necrosis in the interior of the cells not previously described. He says: "The most interesting results were obtained from the examination of the liver. It has long been held that fatty degeneration of this organ was one of the most characteristic lesions of yellow fever, and it was found to a greater or less extent in all of the sections examined. It varied greatly in intensity in the different cases; in some comparatively large areas of liver tissue, which showed very little degeneration, were found; in others only here and there a few normal liver cells were seen. This lesion, however, does not seem to me to be the most important one of the organ. When sections of the liver are deeply stained with eosin and subsequently with a nuclear stain, either hæmotoxylin or methylene blue, a very peculiar appearance results. When such sections are examined with a low power the liver cells are found to be stained a faint reddish blue or purple color, the nuclei being a deep blue or purple. Among the liver cells or in place of them a great number of bodies stained intensely red with the eosin are found when examined with a high power. These bodies are found to differ entirely from the liver cells. They are sharply circumscribed, are highly refractive, and are composed of a perfectly hyaline mass containing numerous vacuoles. Their size varies greatly; in some cases they are no larger than a leucocyte, in others as large as two liver cells. They are found enclosed in liver cells otherwise perfectly normal, and in some cases they entirely take the place of these in the liver beam-work between the capillaries. In some cases examined they apparently made up the mass of the tissue, only here and there a portion of a liver cell or a nucleus of such being seen. Sometimes, especially where the liver tissue was most scanty, along with these definite circumscribed masses more or less granular material was found which stained in the same way. These bodies were generally round or more or less irregular in form. In some of the liver cells small hyaline masses staining in the same way were found which were not so sharply circumscribed as the larger bodies. They were found most abundantly in the cases where the fatty degeneration was most extreme, but the most striking pictures were obtained where the liver was least altered.

"In a few instances liver cells were found which only differed from the normal in being more coarsely granular, the granules staining with eosin, but not so distinctly as the eosin-staining bodies, and the nucleus stained more faintly blue than the nuclei of the surrounding liver cells. In most cases these bodies were without any nucleus; in others a nucleus was present. This always was at the periphery, and generally took the long irregular form of the nucleus of a wandering leucocyte. Polynuclear leucocytes were numerous in all the livers examined. In some cases there were well-defined groups of them in the capillaries and in the liver beam-work between, and as it seemed often in the red-stained bodies. In several specimens there were hemorrhages in the liver, large areas being occupied by red blood corpuscles, between which the red bodies were often seen. This peculiar condition of the liver is possibly made more clear by staining the sections deeply with picrocarmine. In sections so treated these bodies stain an intense bright yellow with the picro-acid. Concerning the nature of these bodies there can be little question. When first seen it was thought that they were probably some form of lower organism, possibly amœbæ, but a more extended study showed that this could not be so. Bodies in all respects similar to them were found in rapidly advancing cases of cirrhosis of the liver, in phosphorus-poisoning, and in other cases of rapid fatty degeneration, but they are particularly found in cases of acute yellow atrophy of the liver. Areas were found in sections from this which were very similar to the advanced cases of yellow fever liver. It must be considered that in yellow fever, along with the fatty degeneration, there is a necrosis of the liver cells which sometimes affects only portions of the cells, at others the entire cell. Almost every change leading up to the formation of these bodies could be seen. The exact relation of the fatty degeneration to the necrosis could not be determined. The necrotic masses were found both in intact liver cells and in those which had undergone fatty degeneration. In the latter cases it seemed probable that the necrosis preceded, or at least accompanied, the degeneration. If it only represented a necrosis of the small remnant of cell protoplasm between the fat drops, it is difficult to see how so large a body could be formed from this. When the necrotic masses were found in the liver cells they were nearly always at the periphery of the cell next to the capillary."[1]

The changes in the *kidneys* are those produced by an acute parenchymatous nephritis. The macroscopic examination does not reveal any marked variation from the normal appearance, except that when a fatal termination has occurred after a very brief illness they may be found hyperæmic and of a deep red color. The observations of Crevaux, Schmidt, and others indicate that there is always a brief period of congestion in advance of the changes in the renal epithelium. Small hemorrhagic foci are not infrequently seen beneath the capsule or in the cortical substance, and little globular hemorrhagic points have been observed on section which proved to be the distended capsules of the glomeruli.

In thin sections, properly prepared, the renal epithelium is found to have undergone degenerative changes to a greater or less extent, and in places complete degeneration has occurred. Sometimes whole bundles of tubes are denuded of their epithelium and are empty. These changes are most marked in the tubules of the labyrinth. Councilman describes the changes in the cells as follows: "The cells often contained larger and smaller fat drops, shown by the clear spaces remaining after they were dissolved out by the alcohol, but the principal change was a hyaline degeneration of the cells. The cells contained an immense number of clear hyaline granules which stained more brightly with eosin. In the dilated tubules there were large and smaller, generally round, masses of similar hyaline material." Besides these hyaline masses there are also granular infarctions of the tubules, and others in which there is a mixture of granular débris and hyaline material. These correspond with the granular and hyaline tube casts found in the urine of yellow fever patients. Again, there are infarctions of another kind which attracted the writer's attention early in his investigations, but the exact nature of which has not been determined. The peculiarity of these consists in their form and in the fact that they are deeply stained by the aniline colors. They are made up of disk-shaped masses, irregular lobate clumps, or amorphous fragments. Councilman speaks of this as "colloid material," and says it is found in the loops of Henle and the collecting tubules. The writer has elsewhere suggested that these infarctions, which are stained by the nuclear staining agents, may be made up of the nuclei of cells which have undergone the hyaline degeneration described by Councilman. Another unexplained object which is not infrequently seen in sections of the kidney has a crystalline appearance and an irregularly circular or lobate outline. These bodies are highly refractive, and are marked by lines of fracture radiating from the centre to the periphery. They do not stain with any of the reagents used in the preparation of sections for microscopical examination. Occasionally a considerable number of leucocytes may be seen in the tubules, and sometimes they contain red blood corpuscles. Councilman concludes his report of the examination of a series of sections which I submitted to him for examination, as follows: "The changes in both the liver and kidney appear to be due to a general toxæmia rather than to the local presence of infectious agents. They are diffuse, affecting the whole of the organs, and not small areas."

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[1] Quoted from the writer's *Report upon the Etiology and Prevention of Yellow Fever*, Washington, 1890, p. 152.

We have heretofore suggested that the phenomena of the disease are due to the action of a deadly toxin formed, probably, in the intestine. My experiments in Havana (1889) show that "the material obtained from the small intestine of yellow fever patients at autopsies made soon after death is very virulent when injected beneath the skin of guinea-pigs."[1] The examination of the liver and kidney for *micro-organisms* has given results which correspond with those obtained by the method of cultivation. In those cases in which my cultures made from blood or liver tissue, obtained as soon as possible after death, gave a positive result, I have usually found the same micro-organisms in thin sections of the same material. In my report, heretofore referred to, I say: "A summary of these results shows that I have obtained micro-organisms in my aërobic cultures as follows: In blood from the heart, 4 times in 19 cases; in the liver or kidney, or both, 13 times in 43 cases."

Dr. Councilman, who carefully examined a series of thin sections submitted to him by me, says: "Bacteria of some sort were found in 28 of the 130 sections examined; of these, 18 were sections of the liver, 8 of the kidney, and 1 each of stomach and lymph gland. There was nothing in their form or relation to the tissue that would lead one to suppose that their presence was other than accidental. In no case could any connection be shown between their presence and the essential lesions of the disease. In no case was there any lesion in the surrounding tissue which could be attributed to their presence. Among the bacilli were some which agreed in form with the colon bacillus."

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[1] *Report on Etiology and Prevention of Yellow Fever*, Washington, 1890, p. 131.

INCUBATION.—The period of incubation is comparatively short, and probably never exceeds five days. Instances of attacks occurring inside of twenty-four hours after exposure are well authenticated. Several authors have insisted that the period of incubation may be prolonged to two weeks or more, but we believe this to be an error based upon a misinterpretation of the facts observed. Thus when a case develops on a ship some time after leaving port, it does not follow that it resulted from exposure while on shore. On the contrary, such a case is usually quickly followed by others, and is evidence that the ship is infected.

SYMPTOMS.—There are no constant or well defined *premonitory symptoms* in advance of an attack of yellow fever, but in a certain proportion of the cases the individual complains of loss of appetite, lassitude, a tendency to perspire upon slight exertion, giddiness or slight headache, and indisposition to make any mental or physical exertion for two or three days before the initial chill, which usually inaugurates an attack. In other cases there is not the slightest intimation of ill health up to the moment of the sudden seizure. This often occurs at night or in the early morning after an uninterrupted sleep. It may also occur during the day while the individual is engaged in his usual occupations. Out of 225 cases in the Roper Hospital, Charleston, observed by Wragg during the epidemic of 1854, the attack was without premonitory symptoms in 92, and in the remainder there was more or less malaise, etc. in advance of the attack.

Although the attack is commonly inaugurated by a decided *chill* or by a slight sensation of coldness, this is sometimes absent, especially in mild cases occurring in the tropics. In certain grave forms of the disease, also, the outset of the attack is insidious and without any noticeable chilly sensation. The temperature is already above the normal, as shown by a thermometer placed in the mouth or axilla, when the patient is suffering from the initial rigor. Accompanying the chill or, in its absence, with the access of fever, there is apt to be more or less *cephalalgia*, which is usually located in the frontal or supraorbital region. The eyeballs also are painful, and there is frequently considerable photophobia. The outset of the attack is also usually accompanied by severe *pain in the loins* and in the calves of the legs, which may continue after the febrile stage of the disease is fully developed. As the chill passes off the temperature rapidly rises; the *face* becomes flushed or of a congested and swollen appearance; the *eyes* are fiery red or shining and suffused; the *skin* becomes dry and hot; and in nervous patients there are great restlessness and jactitation.

The symptoms connected with the onset of the attack as above stated evidently present no features which are peculiar to the disease under consideration, which has, however, a well characterized clinical history when a complete and typical case is considered. In such a case, ending in recovery, we have three tolerably well marked periods: First, a *febrile stage*, which consists of a single paroxysm, lasting usually from forty-eight hours to four or five days, and in which the acme of temperature is reached early in the attack—usually on the first day. Second, the *stage of calm*, which follows defervescence and is marked by great depression of the vital powers, with a slow pulse and sometimes a subnormal temperature. The temperature may, however, remain a degree or two above the normal throughout this stage. Third, the *period of convalescence*, during which the vital forces reassert themselves, and the patient often passes quickly from a condition of extreme danger to one of comparative comfort and safety. In severe cases, however, the stage of calm is usually followed by a reactionary fever of irregular duration which has a more or less remittent character.

Numerous *varieties* of the disease have been described by authors, but yellow fever presents the same clinical features in all parts of the world where it prevails and in different epidemics. The so-called varieties for the most part represent different degrees of severity or depend upon complications and individual peculiarities. Bérenger-Féraud, who had an extended experience in the French Antilles, names the following varieties of the graver forms of the disease: (*a*) ordinary forms, including the gastric, adynamic, ataxic, congestive, and typhoid forms; (*b*) rare forms, including the hyperæsthetic, gangrenous, algid or choleraic, and hydrophobic. In some epidemics death has been known to occur within a few hours of the first manifestations of the disease. These rapidly fatal attacks are classified by French authors as *sidérante*. They are usually algid, congestive, or apoplectic in form, and are most likely to occur in the victims of chronic alcoholism, whose organs have undergone degenerative changes, and are consequently less able to resist the action of the deadly toxin of yellow fever.

The severity of the disease differs greatly in different epidemics. This depends partly upon the character of the population in the invaded area and partly upon local and meteorological conditions. When the population consists largely of negroes or of the creole residents of semitropical countries, the number of cases of the more fatal varieties above mentioned will be comparatively small. Not infrequently, also, the earlier cases in an epidemic are comparatively mild, the poison seeming to gain in activity as the epidemic progresses. Probably in this as in other infectious diseases the severity of an attack depends to some extent upon the dose of the infectious agent introduced into the system at the time of exposure, and this is influenced by conditions which favor its rapid development in the infected localities, especially by accumulations of organic material of animal origin, by heat, and by moisture.

In an account of the clinical history of yellow fever the *temperature* of the body is of prime importance, both as regards diagnosis and prognosis. The acme of temperature is commonly reached within a few hours of the onset of the attack, and rarely later than the evening of the third day. From this time, in uncomplicated cases, the temperature line is a descending one, interrupted sometimes by a slight evening exacerbation, until defervescence occurs, usually in from three to five days. At the end of this *single febrile paroxysm* the temperature, during the succeeding period of depression, may be normal or subnormal, or occasionally a degree or more above the normal. The initial paroxysm is sometimes divided into two or more distinct periods of from two to four days' duration by a more or less complete remission of brief duration, but this is so rarely the case that it does not call for any modification of the general statement that the disease under consideration is a continued fever of a single paroxysm.

"In an analysis of 192 cases recorded by Faget, Jones, and myself the acme of temperature was reached on the first day in 102, on the second in 54, on the third in 33, and on the fourth in 3. The highest temperature recorded by Faget was 107.2° F. Thornton, in a total of 143 cases occurring at Memphis, noted a temperature of 108° F. in a single instance. With this exception, 106.5° F. was the highest temperature recorded by him. In my own observations 106° F. has been the highest temperature noted. The temperature often rises rapidly just before death, and a very high post-mortem temperature (108° F. to 110° F.) is a common phenomenon."[1]

The typical temperature curve may be disturbed by visceral congestions, indiscretions in diet, moving the patient—as from shipboard to hospital—and by excessive fright or grief. The same causes may induce *a relapse* after the termination of the initial paroxysm, as a result of which all the phenomena which characterize this may be repeated, although in non-fatal cases the duration of the febrile movement is usually less.

At the outset of the attack *the pulse* is usually full and strong, the number of pulsations being, as a rule, not more than 100 to 110 per minute. The force and rapidity diminish in a notable manner as the disease progresses, and this early failure in the strength and rapidity of the heart's action, even while the febrile movement is still at its height, is a feature of the disease which, as pointed out by Faget, is of diagnostic importance. During the period of depression—"stage of calm"—which follows the febrile paroxysm the pulse is very compressible and slow, the number of beats falling not infrequently to 40 per minute, and in exceptional cases even as low as 30. This feebleness of the heart's action during the second stage of the disease at a time when the patient often imagines that he is on the high road to recovery, inasmuch as all of his pains and uncomfortable sensations have disappeared, is a very characteristic feature of yellow fever, and one which indicates to the skilled physician a critical condition calling for careful treatment.

The *tongue* presents nothing which is characteristic. Usually it is moist, and becomes quickly coated with a white coating, except at the margins, which remain red. It differs from the tongue of the malarial fevers in being, usually, narrow and pointed, instead of broad and flabby, as is the rule in these diseases. As the disease advances the tongue may become dry and the coating assume a brownish color. In protracted cases it is likely to be very foul and loaded with sordes.

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[1] Quoted from my article in *Reference Handbook of the Medical Sciences*, vol. viii. p. 61.

At the outset of the attack the *face* is flushed or congested and swollen; sometimes in plethoric subjects it may be of a dusky violet color: this, with the deep red suffusion of the eyes which is commonly present in severe cases, together with the absence of any eruption, forms a striking feature of the first period of the disease. The countenance may be expressive of anxiety and pain, but is often dull and apathetic in appearance. Later, in fatal cases, the eyes often become sunken, the eyelids ecchymosed, the brows contracted, and the features shrunken, or the face may be bloated and flabby. In mild cases the hyperæmia of the conjunctivæ and flushing of the face are of brief duration; in more severe cases they often last through the febrile stage of the disease; in rapidly fatal cases the eyes may remain deeply injected throughout. A faint yellowish tinge of the conjunctivæ may usually be recognized by the third or fourth day; this becomes more intense as the disease progresses, and often lasts after convalescence is fairly established.

The skin is sometimes hot and dry throughout the febrile stage; more frequently it soon becomes moist, and free perspiration is readily induced by warm drinks and covering with blankets. During the second stage the skin is usually cool and moist, and when death occurs during this period of depression it is often preceded by a clammy sweat and coldness of the general surface of the body. In exceptional cases the skin remains hot and dry, and the temperature elevated up to the time of the fatal termination, which may be less than forty-eight hours from the inauguration of the attack.

A peculiar odor given off from the surface of yellow fever patients has been recognized by numerous physicians who have had experience in the treatment of this disease, but attempts to describe it have not been very successful. Rush compared it to the "washings from a gun," and Jackson says it is "sickly and faint, and not unlike the smell of a fish-market."

The *yellow color of the skin* which has given the disease the name by which it is generally known among English-speaking people is not always present, or may be so slight as to be recognized with difficulty. In severe cases, however, it is usually seen toward the end of the febrile stage, and becomes more intense during the "stage of calm," lasting until convalescence is fully established and even longer. The color of the skin varies from a faint yellow tint to a deep orange or saffron yellow, or it may occasionally be a bronze or mahogany color. This yellow color is developed at a time when the urine is albuminous and free from bile, and without doubt is due to the presence of blood pigment in the liquor sanguinis and not to bile pigments. But in certain cases jaundice from bile pigments is developed at the end of the second period or during convalescence, and is accompanied by the presence of an abundance of bile pigments in the urine. In these cases the yellow color of the skin is more intense and lasts longer. The characteristic yellow discoloration, which coincides with the period during which hemorrhages are likely to occur, may first be recognized by a slight yellow tinge of the conjunctivæ, of the face, and of the skin over the superficial blood-vessels. In fatal cases the cadaver presents a well marked yellow discoloration, especially the dependent portions subject to pressure, even when this was not noticeable during the last hours of life.

Bérenger-Féraud has noticed an erythematous eruption about the crotum in yellow fever patients which he believes to be a characteristic feature of the disease. Other eruptions mentioned by various authors s occasionally observed are erythematous patches about the knees and elbows, pustules about the mouth and elsewhere, petechiæ, furuncles, etc.

The *urine* is scanty even during the first period of the disease, and n fatal cases complete suppression occurs some time before death. The presence of *albumin* is so constant a symptom as to be properly considered a pathognomonic feature of the disease. In mild cases only a trace may be found during a brief period, but when frequent and careful tests are made it will seldom, if ever, prove to be entirely absent. In cases of moderate severity it is usually present in considerable quantity, especially during the second stage of the disease, when the amount of urine secreted falls to a minimum. In severe cases the coagulated albumin precipitated by heat or nitric acid frequently occupies one half the contents of the test-tube or even more than this. The deposit is usually sufficiently abundant after the second day to leave no doubt as to its character, and increases in quantity during the second period of the disease. The amount present is to some extent an index of the gravity of the attack.

In a series of 16 non-fatal cases in which the writer (1875) made careful observations upon the quantity and specific gravity of the urine the following averages were obtained:

	Fluidounces.	Spec. grav.
First day		1023
Second day	11.5	1025
Third day	16	1028
Fourth day	18	1022
Fifth day	19	1022
Sixth day	20	1022
Seventh day	22	1021
Eighth day	22	1019
Ninth day	23	1016
Tenth day	28	1013
Eleventh day	37	1011
Twelfth day	41	1013

It will be noticed that the amount of urine secreted gradually increased and the specific gravity diminished after the third day. When these two factors are considered together, it will be seen that the total solids excreted were about the same from the third to the eleventh day. The amount of *urea* eliminated by the kidneys is in inverse proportion to the severity of the attack, and corresponds closely with the quantity of urine. This is always considerably less than normal, and in severe non-fatal cases often falls to a few ounces in the twenty-four hours, while in fatal cases complete suppression usually occurs in from a few hours to twenty-four hours before death. According to Cuniset, the amount of *uric acid*, although reduced, is not diminished to the same extent as the urea. The urine, as a rule, has a decidedly acid reaction. Occasionally it contains blood as a result of renal or vesical hemorrhage. In non-fatal cases bile pigments commonly make their appearance in the urine about the time that convalescence is established.

There is usually complete *anorexia* during the febrile stage, and in severe cases this may last through the following period of depression; but in mild cases the appetite usually returns with the disappearance of the fever, and the patient often at once enters upon convalescence. In cases of moderate severity, although the desire for food may return, the stomach is not able to retain anything but the simplest forms of liquid nourishment, and any indulgence of the appetite is likely to cause vomiting and to lead to serious consequences.

Thirst is constant during the febrile stage, and in a less degree during the succeeding period of depression, especially when there is copious and frequent vomiting.

Vomiting frequently occurs during the febrile period, the vomited matters consisting for the most part of fluids ingested, containing in suspension flocculi of mucus from the stomach; occasionally the fluid ejected at the outset of an attack has a yellow color from the presence of bile. The vomited matters almost always have an acid reaction. In cases which run a favorable course vomiting ceases, with the other distressing symptoms, at the termination of the febrile paroxysm; but in severe and fatal cases it is likely to return after an interval of twenty-four hours or more, during which the patient complains of a feeling of weight and discomfort in the epigastric region. This gastric distress may be slightly relieved for a brief period after the act of vomiting, although often nothing is thrown up but a few spoonfuls of a clear acid fluid. In other cases the amount of fluid ejected is considerable; in severe and fatal cases this presents, in a more or less marked degree, the characters of "black vomit." At first the black pigment is usually seen in the form of a few little flocculi suspended in a transparent fluid; in severe and fatal cases the number of these flocculi increases, and the vomited matters may present the appearance known as "coffee-ground vomit," or they may be so numerous as to give the fluid a uniformly black color when first ejected. But upon standing this black vomit usually separates into two portions, the lower containing the black matter in suspension, while above this a transparent liquid is seen. Under the microscope the little pigmented masses are seen, by transmitted light, to have a yellowish brown color, and a careful examination shows that they contain decolorized blood corpuscles and granular leucocytes as well as the brownish pigment granules. In short, there is no doubt that the appearance of black vomit depends upon the escape of blood from the gastric mucous membrane into the cavity of the stomach. Occasionally there is a more active hemorrhage and the patient throws up pure blood. Recovery sometimes occurs after the characteristic black vomit has been ejected, although this is generally recognized as a very grave symptom, presaging death. The name "vomito" given to the disease in Spanish-American countries has reference to the dreaded black vomit, but is scarcely appropriate, inasmuch as a majority of the cases ending in recovery do not present this symptom.

That the gastric mucous membrane is seriously implicated in the disease under consideration is shown by a marked tenderness on pressure over the epigastrium, by the constant feeling of discomfort and pain in the epigastric region in severe cases, and by the tendency to passive hemorrhage above referred to.

The *bowels* at the outset of an attack are apt to be somewhat constipated; later they often remain torpid, but easily moved by a mild cathartic or purgative enema; or there may be more or less diarrhœa during the second period of the disease. In fatal cases the discharges from the bowels are often similar in character to the black fluid ejected from the stomach, and are of the same nature. This may come from the stomach or may be due to a passive hemorrhage from the mucous membrane of the small intestine. Occasionally there is more active hemorrhage and a discharge of pure blood from the bowels. Hemorrhages may also occur from the mouth, nose, bladder, or uterus, or even from the eyes and ears in rare cases. Epistaxis and oozing of blood from the gums, tongue, or lips is the most frequent form of hemorrhage after that from the gastric mucous membrane.

The symptoms connected with the *nervous system* are those which might be expected in a disease characterized by a febrile paroxysm and subsequent stage of depression. At the outset, when the fever is at its height, there is usually severe frontal headache and rhachalgia; the patient is apt to be wakeful throughout the first stage, or his sleep is fitful and disturbed by distressing dreams; his mind is in a state of tension, and he is anxious, watchful, and easily excited; but, as a rule, there is no active delirium. Certain cases are characterized by sluggishness of mental action, apathy, and indifference; in others there are hallucinations and more or less incoherency of ideas; occasionally there is active delirium, which may call for restraint in order to keep the patient in bed, but the intellect often remains unclouded throughout even in severe and fatal cases; more frequently the fatal termination is preceded by a torpid condition of the mind with a disposition to somnolence, gradually passing into complete coma. Occasionally death is preceded by convulsions, and tetanic rigidity of a more or less complete character has been noted as a rare occurrence. There is frequently great restlessness, with deep sighing respiration, often spasmodic in character. The *respiration* is accelerated during the febrile stage, but the respiratory apparatus is not implicated in this disease.

In severe cases convalescence is often slow, and may be complicated by the occurrence of parotitis, abscesses, furuncles, hepatitis, or diarrhœa. In mild cases, on the contrary, the patient frequently is out of bed and ready to resume his usual occupations within a day or two after the termination of the febrile paroxysm. Army experience shows that those attacked are rarely able to resume their duties in a less time than ten days or a fortnight from the date of attack, and that a considerable number must be retained in hospital a month or more, on account of the debility following a severe attack.

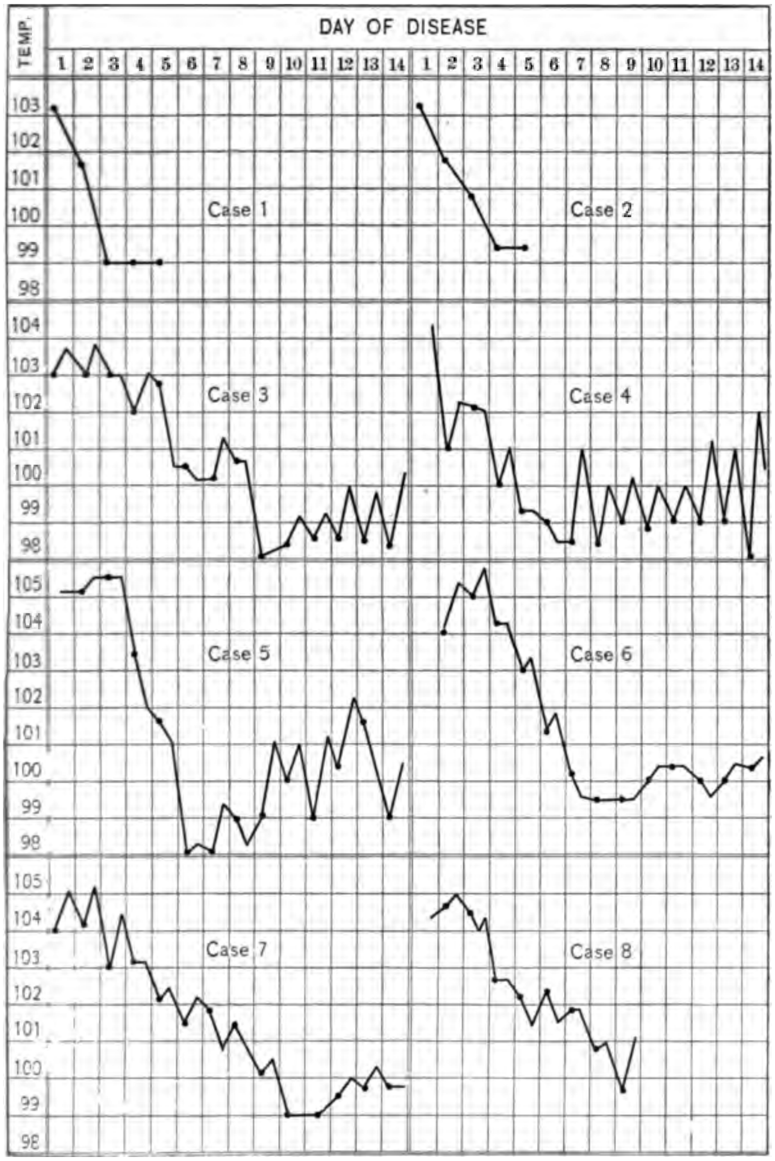
Relapses are not infrequent as a result of some indiscretion committed during the early period of apparent convalescence or during the second stage of the disease. Relapses are said to occur occasionally as late as from two to four weeks after the termination of the primary febrile paroxysm.

DIAGNOSIS.—A prompt diagnosis, especially of the first cases in an epidemic, is often a matter of very great importance. But notwithstanding the well marked clinical features of the disease and its characteristic pathological lesions, the diagnosis of early cases has often been a matter of dispute, even after the autopsy. This may be due to inexperience on the part of physicians encountering it for the first time, or to mistaken ideas as to the nature of the disease among those who have seen much of it, but have failed to recognize its specific character and to differentiate it from certain fevers of malarial origin encountered in tropical or subtropical regions. When a case of yellow fever is improperly diagnosed as "bilious fever" or "remittent fever," and after the administration of several full doses of quinine at the end of three or four days the temperature falls to the normal, the diagnosis is supposed to be confirmed, and this defervescence, which is a characteristic feature of the disease, is supposed to have resulted from appropriate medication. If the case results fatally, the prejudice which so often goes with a positive but mistaken diagnosis sometimes leads to the assertion that the case was one of "pernicious malarial fever." Formerly a considerable number of the physicians in our Southern seaport cities maintained that yellow fever and the malarial fevers are closely allied if not identical diseases, and under this idea the milder cases in an epidemic were often called "malarial fever," and only those in which black vomit and a yellow discoloration of the skin completed the clinical picture of a severe case were recognized as yellow fever. Similar mistakes in diagnosis occur not infrequently at the present day in some of the Spanish-American seaports where this disease is most prevalent.

The fact that the early cases in an epidemic are sometimes of a mild character has led to much confusion in attempts to trace the origin of certain outbreaks. These early cases having been called by some other name, it is not until a typical severe or fatal case occurs that a diagnosis of yellow fever is made: this being considered the first case, the origin of the epidemic which follows remains a mystery, or it is supposed to have originated *de novo* as a result of insanitary conditions which it is not difficult to discover.

There is nothing in the symptoms at the outset of an attack of yellow fever which will justify a positive diagnosis in the absence of a prevailing epidemic. The chill followed by fever, with flushed face, injected conjunctivæ, full pulse, frontal headache, and lumbar pains, might mean smallpox or some other eruptive fever or an attack of one of the malarial fevers. But the eruptive fevers will soon be ruled out by the absence of an eruption; intermittent fever, by the brief duration of the paroxysm and speedy return to a nearly normal state of health; remittent fever after two or three days, by the difference in the temperature curve and the absence of albumin from the urine. It is true that in certain severe forms of malarial fever the urine may contain albumin, but this is not an early symptom in these cases, and does not greatly detract from the diagnostic value of this symptom. In yellow fever, even when the attack is of a mild character, a distinct deposit of albumin will usually be obtained by the third or fourth day, and in cases of moderate severity the precipitate will be so abundant as to justify a positive diagnosis as early as this (third or fourth day) when this symptom is considered in connection with the temperature, the pulse, etc. Or if doubt still exists, the symptoms which characterize the second stage of the disease will serve to differentiate it from those forms of malarial fever for which it has most often been mistaken. As an aid to diagnosis I introduce here several temperature charts of typical cases which show the characteristic features of the febrile paroxysm :

FIG. 31.



Cases Represented by Temperature Charts.

No. 1. Mild case of brief duration; boy, aged three years (New Orleans, 1873); reported by Dr. T. C. Faget.

No. 2. Mild case of brief duration; young female (New Orleans, 1873); reported by Dr. Touatre.

No. 3. Protracted mild case; male, aged twenty-seven years (Fort Barrancas, Fla., 1873); reported by Dr. Sternberg.

No. 4. Typical case of moderate severity; male, aged thirty-one years (Fort Barrancas, Fla., 1873); reported by Dr. Sternberg.

No. 5. Typical severe case; male, aged twenty-seven (Fort Barrancas, Fla., 1873); reported by Dr. Sternberg.

No. 6. Typical severe case; male, aged twenty-seven years (New Orleans, 1873); reported by Dr. Layton.

No. 7. Protracted severe case ending in recovery; reported by Bérenger-Féraud (French Antilles).

No. 8. Fatal case; death on ninth day; male, aged twenty-eight (Fort Barrancas, Fla., 1873); reported by Dr. Sternberg.

It is true that certain cases of malarial fever exhibit a temperature curve which presents considerable similarity to that of yellow fever, but as a rule "remittent fever" has a series of febrile paroxysms separated by more or less complete remissions, instead of a single paroxysm of several days' duration ending in defervescence, complete or nearly so.

As regards the presence of albumin in the urine, the following observations by Donnet, made during an epidemic in Jamaica, are of interest: In 61 cases, carefully studied, albumin was found for the first time on the first day in 2; on the second day in 11; on the third day in 19; on the fourth day in 14; on the fifth day in 6; on the sixth day in 4; on the seventh day in 4; on the eighth day in 1.

The desquamative nephritis to which the presence of albumin is due is also shown by the presence of numerous granular casts in the urine, which may usually be found as early as the third or fourth day.

If a diagnosis has not been made before, the symptoms which characterize the second period of the disease should serve to differentiate it from all forms of "malarial fever," properly so called. The cool and usually moist skin, the abnormally slow, soft pulse, the gastric distress and pain or pressure in the epigastrium, the yellow tinge of the conjunctivæ, and the albuminous urine in a patient whose temperature is normal or subnormal, following a febrile paroxysm such as is represented by our temperature charts, certainly furnish a clinical picture which should be recognized. But experience shows that it frequently is not recognized, and cases which present the additional feature of black vomit have been called "hemorrhagic malarial fever," "pernicious fever," etc.

It is true that severe cases do not always present the typical course which we have described: the temperature may remain a degree or two above the normal during the stage of depression; the skin may be dry, and a reactionary fever of a remittent character may quickly follow the initial paroxysm; but we still have the albuminous urine, the abnormally slow pulse, the yellow tinge of the conjunctivæ, and in certain cases the hemorrhages so common in this disease—black vomit, etc. In addition to this there are other differences in symptoms which have more or less value. The tongue in yellow fever is usually narrow and pointed, with red margins, and is apt to be tremulous; it is often comparatively clean at the outset, and rarely presents the thick yellowish or brownish coating seen in remittent fever. The tongue in the malarial fevers is usually broad and flabby, and marked upon its margins by indentations made by the teeth. The yellow color of the skin in bilious remittent fever is due to a staining by bile pigments, and does not differ from that of simple jaundice; it is more intense in color and more persistent than the yellowish tint seen in yellow fever: it should be remembered, however, that a true biliary jaundice may be developed in non-fatal cases of yellow fever during the period of convalescence.

The spleen is not involved in yellow fever, while in the malarial fevers it is more or less swollen and tender. Vomiting of bilious matter is a common symptom in severe forms of malarial fever; in yellow fever it is rare, and only occurs, if at all, at the outset of the attack; the vomited matters later are transparent and colorless. In yellow fever the amount of uric acid excreted is diminished, while, according to La Roche, it is notably increased in remittent fever. Suppression of urine is a common feature in fatal cases of yellow fever; it rarely occurs in bilious remittent fever.

That form of fever which the French denominate *fièvre bilieuse mélanurique*, and which has been called "hemorrhagic malarial fever" by certain American authors, presents features which differ essentially from those of yellow fever. These are well stated by Bérenger-Féraud, as follows:

"Prolonged residence in a malarial country is the most powerful, and, indeed, indispensable, predisposing cause.

"The disease is always preceded by numerous attacks of malarial fever, simple at first, then more and more complicated, and taking on in general more and more of a bilious aspect, producing a very decided anæmia.

"Icterus appears at the outset of the attack, and is never wanting; it gives from the commencement and throughout the attack a uniform yellow color to the patient, varying from greenish yellow to a decided yellow ochre.

"The march is intermittent or remittent from the first, and the pulse, urine, and vomiting follow very exactly the variations of temperature.

"The vomiting is bilious, of a decided green color; it is a constant symptom at the outset of an attack, and is arrested with the termination of one attack to reappear with the next.

"After the first, or febrile, period the vomiting continues, but preserves the same characters; it stains linen a bright green, and when collected in a basin it appears transparent and is of a beautiful emerald green or olive color.

"The tongue is moist, broad, covered at first with a heavy white fur, which soon receives a greenish tint from the vomited matters. The tongue is not red, either upon its tip or edges; it remains broad, heavily coated, and moist to the end of the malady.

"The urine is black from the commencement, and its color is characteristic, so that the patient himself is struck with it. It is usually abundant and frequently passed, and only has the melanuric aspect during the attack."

Dengue, as regards its epidemic prevalence, somewhat resembles yellow fever. It is an acute, infectious disease, which prevails in those latitudes which are most subject to invasion by yellow fever during the season most favorable for the epidemic extension of this disease. It, also, is characterized by a febrile stage of comparatively short duration, but the characteristic features of yellow fever are absent—albuminous urine, stage of depression, hemorrhages, etc.—and it is accompanied by severe arthritic and muscular pains which have led to its being called "breakbone fever." Moreover, there is usually a well marked eruption, resembling that of scarlet fever and commencing on the third day, and after the termination of the initial febrile paroxysm a second commonly occurs, accompanied by a rubeoloid eruption which often ends in desquamation of the cuticle. There is a wide difference also in the comparative fatality of the two diseases. Dengue, although the most distressing to the patient, is by far the least serious in its results, and rarely is the cause of death.

Certain circumstances connected with the personal history of the patient will aid greatly in establishing an early diagnosis. A stranger in Havana or Rio de Janeiro during the epidemic season, who has an attack of fever presenting the symptoms described as attending the febrile stage of this disease, and whose urine is found at the end of two or three days to be albuminous, is sent without hesitation to the yellow fever hospital. And a person arriving at one of our seaports from an infected locality, presenting similar symptoms, would be isolated and placed under careful observation, even if the diagnosis was not at once established. But in a similar case, with no history of exposure in an infected locality, there is often doubt as to the diagnosis or an absolute denial of the possibility that the disease is yellow fever.

When we hear of the prevalence of a "malignant form of malarial fever" in a seaport city located within the limits of yellow fever invasion, we are always justified in suspecting that the disease is in fact yellow fever. For malignant and fatal forms of malarial fever belong to the country rather than to the city, and cases of this kind do not occur in groups among the residents of a restricted area within the limits of a city. Even when a localized epidemic does not appear to be "malignant" in character, especially when it occurs among a native creole or negro population, the fact of its prevalence in a large town or city is opposed to the view that it is of malarial origin—properly so called—and it is more likely to be yellow fever than anything else, unless, indeed, it should prove to be dengue.

PROGNOSIS.—Yellow fever is an extremely fatal disease, and even in apparently mild cases a guarded prognosis should be made, as they may suddenly assume a serious character. The prognosis is especially unfavorable in the case of plethoric persons and in those of intemperate habits. It is more favorable in women and children than in men—more favorable in the case of native creoles and negroes, in warm latitudes where the disease prevails, than for recently arrived strangers from more northern latitudes.

The writer's personal observations and studies have led him to attach great value to the temperature observations made during the first two or three days of the attack as a guide in prognosis. When the temperature of the body, as shown by a clinical thermometer placed in the mouth or axilla, does not go above 103° to 103½° F. during the first forty-eight hours, a favorable result may usually be anticipated. If, on the contrary, the temperature reaches 105° or more, the case must be considered a severe one and the prognosis is grave. This is shown by the following table, compiled by the writer some years since from a series of 269 cases recorded by various authors, in which careful temperature observations had been made:

Cases in which the temperature was	No. of cases.	No. of deaths.	Percentage of deaths to cases.
107° and above	13	13	100
106°–107°	9	9	100
105°–106°	36	22	61
104°–105°	80	24	30
103°–104°	87	6	7, nearly
102°–103°	29	0	
101°–102°	15	0	
Total	269	74	27.5

The amount of urine secreted and the quantity of albumin it contains will also furnish an important prognostic indication. However favorable the symptoms may appear otherwise, if the urinary secretion is scanty and it is heavily loaded with albumin, the case is a grave one. On the other hand, great depression, black vomit, or hemorrhages are not necessarily fatal symptoms, and hopes of recovery may be entertained if the urinary secretion is satisfactory in amount and the quantity of albumin small. Great distress and tenderness in the epigastric region, with frequent vomiting, are unfavorable, as is great restlessness with sighing respiration or delirium. The early appearance of the hæmatogenous jaundice characteristic of the disease is not favorable.

The *mortality* differs greatly in different epidemics, and, as heretofore pointed out, depends largely upon the character of the exposed population. Where a considerable proportion of those attacked are children, native creoles, or negroes, the mortality is comparatively low—from 5 to 10 per cent. But among unacclimated male adults the mortality is rarely less than 20 and frequently above 50 per cent. The mortality in the great epidemics which occurred in Philadelphia at the end of the last and commencement of the present century was from 20 to 80 per cent. The mortality in the seaman's hospital at Georgetown (Demerara) in 1838 was 19.5 per cent. (Blair). The mortality at Vera Cruz during the seven years ending 1881 was 41 per cent. in the hospital for women and 41.48 per cent. in the hospital for men (Molina). In 1855 the mortality among the Spanish stroops in Cuba was 24.31 per cent. In 1873 the mortality in Rio de Janeiro was 23.3 per cent. In the epidemic of 1878, 27,000 cases and 4600 deaths occurred in the city of New Orleans (17 per cent.); 18,500 cases and 5000 deaths in Memphis (27 per cent.); at Vicksburg 5000 cases and 872 deaths (17 per cent.) — 2000 cases and 231 deaths among the colored population. These figures are from the report of a "Board of Experts" appointed by Congress to investigate the epidemic. The total number of cases and deaths collected by the Board, as occurring in 132 cities and towns in the infected area, was—cases 74,265; deaths 15,934 (besides 254 "reported without any report for the number of cases corresponding thereto"). This gives a mortality of a little over 21 per cent. for the entire epidemic. These figures, however, are only approximate, and no doubt the mortality rate would be reduced somewhat if all of the cases had been reported. It must be remembered also that the figures relate to both the white and colored populations, and that in many localities the negro population was equal to or in excess of the white population, as many of the latter class deserted their homes and sought refuge in healthy places farther north. Bemiss has given the following table showing the mortality according to age, among whites only, during this epidemic. The figures include the cases treated in private practice by four of the leading practitioners of the city of New Orleans:

Age.	Cases.	Deaths.	Per cent.
Under 5 years of age	206	26	12.67
From 5 to 10 years of age	233	20	8.58
From 10 to 20 years of age	183	9	4.9
From 20 to 40 years of age	232	39	16.7
From 40 to 60 years of age	47	6	12.7
From 60 to 80 years of age	4	2	50.0
Total	905	102	11.28

The day of death, as ascertained in 1059 fatal cases occurring in the French Antilles, is given by Bérenger-Féraud as follows: On the second day of sickness, 16 (1.5 per cent.); on the third day, 56 (5.3 per cent.); on the fourth day, 141 (13.4 per cent.); on the fifth day, 165 (15.7 per cent.); on the sixth day, 177 (16.9 per cent.); on the seventh day, 151 (14.3 per cent.); on the eighth day, 89 (8.5 per cent.); on the ninth day, 42 (3.9 per cent.); on the tenth day 35 (3.3 per cent.); on the eleventh day, 28 (2.6 per cent.); on the twelfth day, 34 (3.2 per cent.); on the thirteenth day, 25 (2.3 per cent.); on the fourteenth day, 21 (1.9 per cent.); on the fifteenth day, 8 (0.7 per cent.); on the sixteenth day, 7 (0.6 per cent.); on the seventeenth day, 13 (1.2 per cent.); on the eighteenth day, 6; nineteenth day, 6; twentieth day, 7; twenty-first day, 3; twenty-second day, 2; twenty-third day, 5; twenty-fourth day, 3; twenty-fifth day, 3; twenty-sixth day, 5; twenty-seventh day, 1; twenty-eighth day, 1; twenty-ninth day, 2; thirtieth day, 1; thirty-first day, 3; thirty-second day, 1; thirty-third day, 1; thirty-sixth day, 1. Out of the total number of deaths, 67 per cent. occurred during the first week and 82 per cent. during the first ten days of sickness. This corresponds closely with the results obtained by Surgeon Clements as regards 111 fatal cases occurring in the U. S. Army. Of these, 73 per cent. died during the first week and 82 per cent. during the first ten days.

TREATMENT.—All attempts to "cure" yellow fever by a specific treatment have been unsuccessful, and those physicians who have had most experience in the treatment of the disease generally agree that active medication, except for the purpose of meeting symptomatic indications, is mischievous. But it is possible that a specific treatment may yet be found, and further efforts should be made in this direction. Reasoning from analogy, it seems probable that the immunity which results from an attack of yellow fever is due to the presence of an antitoxin in the body fluids of the immune individual. And if this antitoxin could be utilized for the protection of exposed individuals or for the cure of those already attacked, its specific power might be manifested. But in the present state of knowledge there are serious difficulties in the way of testing the possible efficacy of such a specific mode of treatment. The specific infectious agent not having been demonstrated, and no one of the lower animals having been shown to be susceptible to infection, the only method which suggests itself for obtaining a supply of antitoxin is to tap the veins of an immune person for the purpose of obtaining blood serum to inject into the yellow fever patient. It is to be hoped that the experiment will be made at as early a date as possible, as the result would be of great scientific interest, and if favorable some method of more general utility might be discovered.

The idea that yellow fever is closely allied to the malarial fevers, which at one time was entertained by many physicians in regions subject to invasion, led to the attempt to abort the disease by the use of quinine in large doses. This experiment has been fully tried, and the treatment abandoned by most physicians of experience. Some, however, still think that a large dose of quinine (20 to 30 grains), given at the outset of the attack, has a favorable effect in modifying the severity of the febrile paroxysm and allaying nervous excitement. On the other hand, it is generally admitted that it sometimes induces cerebral congestion, and that a repetition of the dose may lead to unpleasant results. Blair, who had an extended experience in the British West Indies, was in the habit of giving 20 grains of calomel and 25 grains of quinine at the outset of an attack, and in certain cases the dose was repeated. Dr. Porcher of Charleston approves of Blair's treatment so far as the first dose is concerned, but protests against its repetition. The amelioration of the symptoms which has been ascribed to this dose may be due in part to the antipyretic action of the quinine, but the free movement of the bowels usually induced by the calomel is entitled to at least a portion of the credit. It must be remembered also that the natural tendency of the disease is in the direction of a more or less prompt defervescence, and that the acme of febrile action, with its accompanying headache, pain in the loins, etc., is reached very soon after the inauguration of the attack. This amelioration of the symptoms attending the onset of the disease has no doubt often been improperly ascribed to the medicine administered, and the novice in the treatment of this disease is apt to congratulate himself upon the success of his treatment when the patient is in reality in the greatest danger—a danger which may be the greater as a result of over-active medication, by which the sensitive stomach is apt to be disturbed, the weak heart still further enfeebled, and the inflamed kidneys taxed beyond their power of resistance.

In the days of "antiphlogistic treatment" *emetics* were considered an important element in this treatment, and it was part of the routine to administer them at the outset of every case. This is still the practice with certain of the South American physicians. When the stomach contains undigested and fermenting material which causes nausea and distress, it is well to aid the efforts of nature by the administration of a simple emetic, otherwise it is not likely to do any good, and we do not approve of its routine use. *Purga-*

tives are generally believed to be useful at the outset of an attack, and most physicians commence the treatment by giving some medicine to promptly unload the bowels. Opinions differ as to the best form of cathartic medicine, but preference is given by many to a full dose of oleum ricini. On account of its non-irritating properties and prompt action it is a favorite in our own Southern cities, in the West Indies, and in Brazil. From two to four ounces are commonly given to an adult in a single dose. Experience shows that this is not excessive and that it has a prompt and favorable action. Some physicians prefer a mercurial, followed, if necessary, by a saline cathartic, and calomel is still the favorite with many. One reason for promptly emptying the *primæ viæ* is found in the fact that later the administration of cathartic medicine is likely to do harm by inducing vomiting difficult to control, and by increasing the depression which follows the febrile paroxysm. If it seems desirable to move the bowels after the second day of the disease, this had better be done by a purgative enema.

In the present state of knowledge a carefully managed *symptomatic treatment* will give the best results attainable and will do much toward reducing the mortality. We have pointed out the fact, in speaking of prognosis, that the temperature of the body, as shown by the clinical thermometer, is a fair index of the severity of the attack. It does not follow from this that the high temperature in severe cases is, *per se*, a cause of danger. If this were true, the evident indication would be to keep down the temperature by means of cold baths or antipyretic medicines. The intensity of the pathogenic action of the specific poison is indicated by the height and duration of the febrile movement, but we do not neutralize the pathogenic action when we reduce the temperature of the body. In the malarial fevers the temperature frequently rises to a higher point in cases which are not attended with any special danger. Nevertheless, it is desirable that this symptom—high temperature—should receive appropriate treatment, and a reduction of the febrile heat is usually attended with an amelioration of other more or less distressing symptoms—thirst, headache, sleeplessness, jactitation, etc.

The use of the cold bath is not to be recommended, unless it should be at the very outset in a case presenting an unusually high temperature with evidence of cerebral congestion. The tepid bath is better, but the most judicious and experienced practitioners in yellow fever regions agree that it is better not to disturb the patient to the extent necessary in administering frequent baths, and that after the first twenty-four hours, at least, they had better be omitted. The object in view may be accomplished with less disturbance to the patient by frequently sponging the hands, arms, and chest with cold water or with an evaporating lotion. Bérenger-Féraud recommends a mixture of 1 part of "aromatic alcohol" with 3 parts of water. Porcher advises the "assiduous and protracted application of ice-cold water to the head, hands, and arms as long as they are abnormally hot." Some practitioners are afraid of cold water and prefer to sponge the surface with tepid water. In our judgment, cold water and evaporating lotions may safely be used as applications to the head and for sponging the surface so long as the skin is hot and dry and the temperature elevated. When, however, the febrile stage is approaching its termination, it will be prudent to discontinue the sponging of the surface or to use tepid instead of cold water, on account of the great tendency to visceral congestions at this time. A hot mustard foot-bath is very commonly administered at the outset of the attack in domestic practice and by many physicians of experience. This may be repeated several times during the first twenty-four hours, and often induces a free perspiration, with relief of the headache and other distressing symptoms which occur at this time. The usual procedure is to have the patient sit upon the edge of his bed with a blanket wrapped around him and his feet and legs immersed in a bucket of water as hot as he can bear and containing a liberal quantity of mustard flour.

Bérenger-Féraud recommends the use of large enemata of cold water as an antipyretic measure. These may be frequently repeated, and are said to be quite harmless. Cold enemata have also been recommended for the relief of the congested and inflamed kidneys.

The knowledge that exposure to cool currents of air or a sudden fall in the external temperature is dangerous for yellow fever patients on account of the visceral congestions which are likely to be induced by such exposure—especially of the kidneys—has led many physicians to refrain from the use of cold lotions to the surface as an antipyretic measure, and by some the use of cold drinks is denied. This we believe to be a mistake, and the excessive use of blankets and hot drinks to induce perspiration may cause great discomfort to the poor patient without any corresponding benefit. When the febrile stage is approaching its termination, and during the stage of depression which follows, exposure to cold currents of air or a sudden fall in the external temperature, not compensated by artificial heat or a sufficient supply of bed-covering, may be fatal. But when there is considerable fever the patient should be lightly covered, care being taken, however, to protect him from draughts. If the skin is hot and dry, warm aromatic drinks may be given to promote perspiration, but it is a mistake to suppose that the course of the disease can be arrested or the deadly poison eliminated by maintaining a free perspiration; and when the patient is loaded down with blankets, the profuse perspiration which is often induced by this treatment does not materially reduce the body heat. *Antipyrine* has been given for its sedative and antipyretic effect, and is considered useful by some of those physicians who have had an opportunity to test its value. We should be disposed to administer it with caution and during the acme of febrile heat only—preferably at night, with a view to securing rest.

The use of arterial sedatives in small but repeated doses is approved by many experienced physicians: they may reduce the febrile action to some extent. *Aconite* may be given in combination with some mild diaphoretic during the first day or two; later, *digitalis* will be preferable on account of the tendency to heart failure. Bemiss says: "We have seen digitalis produce unquestionably good effect in mitigating fever, and have often administered it in doses of thirty to sixty drops of the tincture every third or fourth hour. It is best to give it in solutions of acetate of ammonia or potash." We should prefer to give it, in proper doses, with a solution of sodium bicarbonate in ice-cold water, administered as recommended by the writer in 1887.

Bicarbonate of soda has frequently been prescribed as an occasional dose to neutralize the acid secretions of the stomach and to allay vomiting, but in the treatment above referred to the writer proposed, by the systematic administration of this salt, to neutralize the acid secretions from the outset, and thus to prevent, if possible, the nausea and vomiting which are so frequently distressing features of the disease. An alkaline treatment seemed to be indicated also by the highly acid condition of the urine, and it was hoped that it might have a favorable action on the kidneys. And on theoretical grounds it was thought that it might be well to administer at the same time the powerful antiseptic, mercuric chloride, in a minute and perfectly safe dose. Accordingly the following prescription was made:

℞. Bicarbonate of soda,	10.	(150 gr.).
Bichloride of mercury,	0.02	(⅓ gr.).
Pure water,	1000.	(1 qt.).

M. Sig. 50 cc. (3 tablespoonfuls) every hour; to be given ice-cold.

Another object in view was to give a moderate quantity of ice-cold water at regular intervals, as this would be less likely to induce vomiting than larger amounts taken at the patient's option, and if absorbed would quench thirst better than larger quantities quickly rejected. I have had no personal experience in the treatment of yellow fever since this plan was suggested, but have received very favorable reports as to its value from various sources.

The treatment referred to has been tested by a number of physicians in the United States, in Cuba, and in Brazil, and I have had reports of 374 cases treated by ten physicians. Of these, 301 were whites, with a mortality of 7.3 per cent. and 73 cases blacks, with no mortality.

During the last epidemic at Jacksonville, Florida (1888), Sollace Mitchell treated 106 cases in the "Sand Hills Hospital" with 5 deaths—a mortality of 4.7 per cent. Of the 106 cases, 79 were whites, and of this number 73 were adult males. All of the deaths occurred among these, and the mortality among this class, considered separately, was 6.8 per cent.

La Guardia and Martinez in 1889 treated 44 cases in the Mercedes Hospital, Havana, with a mortality of 15.9 per cent. They say: "We have observed the following facts: The patients have offered a notable gastric tolerance during the medication; when treated from the first day vomiting has rarely occurred. The secretion of urine has always been considerable; even in the grave cases, when death occurred, they did not die anuric." Whether this treatment is still in use in the Mercedes Hospital and elsewhere in the city of Havana I am not informed, but the evidence published is certainly sufficient to justify a more extended trial. To what extent the small amount of mercuric chloride added to the formula is concerned in the favorable results reported I am unable to determine. This salt remains in solution in presence of sodium bicarbonate, but would be precipitated by potassium carbonate, which salt is also contraindicated in a disease in which there is a tendency to uræmic poisoning.

The addition of tincture of digitalis in suitable doses to the formula given might prove to be an advantage, but this can only be determined by carefully conducted clinical experiments. The administration of the ice-cold alkaline mixture at regular intervals, with or without the addition of one of the agents mentioned, appears to us to be a rational feature in the symptomatic treatment of the disease, and, as stated, is supported by favorable clinical evidence.

It is very desirable to prevent vomiting, inasmuch as the attempt to arrest it by medicines administered *per os* is usually a failure. Morphia given hypodermically suggests itself, but experience shows that this is a dangerous remedy, and only very minute doses are tolerated. Blair has seen stupor, prostration, and complete narcotism follow the administration of one tenth of a grain. We agree with him that it should be placed in the *index expurgatorius* so far as yellow fever is concerned.

Diuretics appear to be indicated on account of the scanty secretion of urine, but experience teaches that they are of little value, and that it is better to relieve the strain upon the hyperæmic and inflamed kidneys by diaphoretics and revulsants than to attempt to stimulate them to greater activity. When there is a tendency to suppression the application of large mustard poultices to the loins and the use of cold water enemata, together with measures appropriate to maintain a free transpiration by the skin, will be more likely to give relief than any diuretic medicine. After complete suppression has occurred no method of treatment is likely to be of any avail. Where the skin is hot and dry and the urinary secretion scanty, it might be worth while to administer a hypodermic injection of the muriate of pilocarpin (0.008 to 0.016 gm. = $\frac{1}{8}$ to $\frac{1}{4}$ grain). Hebersmith reports that when given in this way the dose mentioned produces a profuse perspiration with reduction of temperature.

Cerebral congestion is best relieved by cold applications to the head and *sinapisms* applied to the extremities. The feeling of weight and distress in the epigastric region, attended with nausea and due to hyperæmia of the gastric mucous membrane, also calls for the local application of cold—best secured by swallowing bits of ice or small quantities of ice-cold water, which may be charged with CO_2—and for revulsion to the surface by sinapisms applied to the epigastrium. These often give great relief, and are to be preferred to vesicants, which have no special advantage over sinapisms for the relief of the symptoms referred to, while the blistered surface gives much distress to the patient after it has ceased to do any good as a revulsive.

Stimulants are of the greatest utility in the second stage of the disease to sustain the feeble heart. They are rarely required before the fourth day, and should be given in small amounts, so as not to provoke vomiting. A little iced champagne will often be retained when the stomach rejects everything else, or brandy given ice-cold and with the addition of very little, if any, water, may be given in teaspoonful doses at short intervals. Later, when the patient enters upon convalescence, milk punch, English ale, or a sound wine may be given in liberal quantities. Blair prefers Rhine wine, and says: "When of good quality it is retained when everything else is rejected, and is universally liked by the patients. The happy effect of the judicious use of stimulants is shown not only by increased force and rapidity of the heart's action, but frequently by a relief of the distressing nervous phenomena often present during the stage of depression—sighing respiration, sleeplessness, jactitation, hiccough. There is a tendency to syncope during the second stage of the disease, which is especially manifest during the latter part of the night, when the powers of nature seem to be at the lowest ebb. This is often fatal, especially when the nurse or physician is not at hand to administer the stimulant which is so essential for the rescue of the patient at this critical moment."

Hemorrhage from the nose, stomach (black vomit), or bowels will often resist all treatment. An effort should be made to arrest it by the administration of ergotin by the hypodermic method, as some authors have reported favorable results from this treatment.

During convalescence, which is often protracted after severe attacks, tonics will be found useful, and especially the salts of quinine, strychnine and iron, either separately or in combination.

The *alimentation* in cases of yellow fever requires special attention. The stomach for some days is not in a condition to digest any food: during the first part of the febrile stage the patient usually has no desire for food, nor should any be given him. In mild cases there will often be a demand for food as soon as the fever subsides, but great caution must be exercised in complying with this demand. At first only the simplest forms of liquid nourishment should be permitted, and milk or chicken broth will usually be found the most acceptable to the patient and the least apt to disturb the stomach. In severe cases with much gastric irritability the milk should be mixed with lime-water and given at first in quantities not exceeding a tablespoonful, at intervals of an hour or two. If this is not retained, nutritive enemata should be administered, and the stomach should be given a further period of complete rest. When liquid food is retained and assimilated, it should be given in moderate quantities at intervals of two or three hours for a couple of days in mild cases, and for a longer time in those of a more serious nature, after which the simplest forms of solid food may be cautiously given. It should be constantly borne in mind, however, that premature indulgence in solid food is a frequent cause of relapse, and that relapses are extremely fatal.

CHOLERA.

BY JOHN M. BYRON, M.D.

DEFINITION.—Cholera is an exceedingly acute infectious disease, caused by the action of a pathogenic germ—the cholera spirillum, or comma bacillus of Koch—and characterized by a group of clinical symptoms, the most striking of which are vomiting, very profuse watery dejecta, muscular cramps, rapid emaciation, anuria, asphyxia, and collapse.

SYNONYMS.—Cholera Asiatica; Cholera maligna; Cholera infectiosa; Cholera algida; Epidemic cholera.

"*Cholerine*" is an unscientific term which is indefinitely used to describe either mild cases of Asiatic cholera in which the stage of collapse is cut short, or more frequently it is applied to those cases of severe and usually fatal diarrhœa or gastro-enteritis which are apt to prevail during a cholera epidemic or to precede or follow it. The latter use of the word was common in France in the epidemic of 1892–93, and large numbers of cases of this type were recorded in Paris and other cities.

HISTORY.—The epidemiology of cholera is an interesting study, but an elaborate discussion of the history of recent epidemics must give place in this work to brief mention of the more important ones. It has long been known that cholera in its invasion of countries follows only the well-worn routes of travel, both by sea and land, and that it never proceeds faster than the ordinary means of communication between different towns. The disease has doubtless been known for very many centuries under the general names of plague or scourge, but intelligent accounts of it are not to be found earlier than those of the tenth century. Cholera undoubtedly owes its birthplace to India, chiefly in the delta of the Ganges, and in that country it is endemic, affording a nursery from which, at irregular intervals, it is widely transplanted and disseminated through neighboring Asiatic countries and Europe. The invasion of India by foreign peoples has done much to extend the original limits of the disease, and the more peaceful invasions of today through pilgrimages, especially to Mecca and Medina, afford the most favorable conditions for its spread. An epidemic starting near Bombay or Calcutta will oftentimes spread in several different directions, invading China, Japan, Ceylon, the Philippines, and other islands of the Eastern Archipelago. At the same time it may extend westward into Persia, Turkey, Egypt, and adjoining countries, also passing across the Black and Caspian Seas and entering Russia. It may even extend to St. Petersburg. The disease is carried along the Mediterranean shores, giving rise to outbreaks in Italy, France, Spain, and different African states. It may progress thus far in a single year, or two or three years may be occupied in reaching these limits. Unless the epidemic is checked it extends to Germany, and occasionally into England. Having reached such ports as Naples, Hamburg, or Havre, it is brought across the Atlantic to the United States, to the eastern coast of South America, Mexico, and Cuba, whence the United States may be again invaded through the States bordering on the Gulf. This is a brief outline of what has been the progress of many epidemics. Fortunately, these epidemics are often cut short, apparently more from the disease itself dying out from natural causes than from any influence of sanitation, which is still so imperfect in most Eastern countries.

For many centuries epidemics were recorded recurring at intervals in India, Mesopotamia, Persia, Egypt, Turkey, and adjacent south-eastern Russian provinces. The sacred city of Hundwar is the special nursery from which epidemics have started for invasion of Western European countries. Throughout India the filthy habits of the natives are most favorable to the dissemination of cholera. Many of their religious customs, especially in regard to bathing, and their indulgence in pilgrimages to sacred shrines, during which they live under conditions of overcrowding and fatigue, predispose them to contracting the disease. In Mecca as many as 150,000 sheep may be slaughtered annually for religious ceremonies, and their entrails are allowed to decompose on the hot ground. The irregularity in the water supply of the country necessitates its storage in large pools and tanks, which for the most part are entirely unprotected from sewage and excreta, the same tank being often used for drinking purposes, bathing, and the washing of food utensils. Such water, once contaminated with a few cholera germs, may spread the disease among thousands of people in an incredibly short time. In large overcrowded cities of India and China methods of modern sanitation are almost wholly unknown.

In 1817 a widespread epidemic of cholera originated in India, passing southward from Calcutta and embracing Central India, Ceylon, Madagascar, and China. It also passed eastward and afflicted Delhi and Damascus and other Eastern cities, and was carried across the Caspian Sea to Astrakhan. Eventually, the epidemic involved almost the whole of Asia, but it did not invade Europe. Nine years later another epidemic, likewise originating on the Ganges in the neighborhood of Calcutta, spread over very much the same route, but penetrated into Southeastern Russia and reached as far as Moscow. By other routes the plague penetrated Austria-Hungary, visiting Poland, finally attaining to St. Petersburg and the principal capital cities of Europe, including Bremen, Hamburg, Paris, and Madrid; some cases also occurred in London. Shortly afterward another epidemic passed from the Ganges into Arabia, Egypt, and European Turkey.

Another decided outbreak of cholera occurred in Eastern Europe in 1832, making frightful ravages, and causing 120,000 cases in France alone. In this year also the disease first reached the United States, being brought over to Quebec in an emigrant vessel from Ireland, and spreading thence to New York City and elsewhere in the United States. Three thousand five hundred victims met their death in New

York City alone. It was carried to Cuba, and then back again to the United States through New Orleans.

In 1840 a severe epidemic, originating, like all the others, in the vicinity of the Ganges, penetrated China and the Eastern Archipelago. It also again invaded Europe both by land and from the Mediterranean ports, and finally reached New York by the way of Havre in November, 1848.

In 1849 another invasion of cholera afflicted this country, entering by the way of New Orleans. Having once obtained a foothold, it extended as fast as the various means of travel allowed, and the year following 5000 deaths took place in New York.

A similar widespread epidemic, originating in 1851, involved all the European countries, and entered the United States in the two successive years 1853 and 1854. From this epidemic 2000 more deaths were recorded in New York City.

In November, 1865, New York was once more invaded, the disease having travelled the usual route from India along the Mediterranean, through France to Havre. Eight years later it was again brought into the United States by the way of New Orleans, and it passed on to South America.

A few cases appeared again throughout the United States in isolated localities in 1873, but a general epidemic was prevented by the fact that the disease was better understood, and it was soon stamped out by active sanitary measures. In 1883 an epidemic in Egypt gave rise to 50,000 deaths, and, according to Parke, more than 600 natives died daily in Cairo. In the same year another epidemic, starting from Bombay, was cut short at New York Quarantine, which it reached four years later.

Another pandemic fluctuated between various European cities in 1884 and 1887, making its way eventually to Paris. In 1886–87 one of the largest South American epidemics occurred, and 22,000 deaths took place in Chili. In 1890 the disease prevailed with some severity in widely separated regions of the globe, principally in India, Japan, China, Asiatic Turkey, Italy, Spain, Natal, and Abyssinia.

In the winter of 1891–92 cholera appeared in isolated towns in Persia, and in 1892 an epidemic wave started from Meshed in Persia, and followed the line of the Transcaucasus Railway into Russia, finally reaching Nijni-Novgorod, Moscow, and St. Petersburg. The disease also broke out in Havre and Hamburg, though by what means it reached these cities has never been clearly established. In the spring of this same year a number of patients died in Paris and elsewhere in France of gastro-intestinal symptoms, which were, however, reported under the name of "cholerine." About this time the disease invaded Russia along the borders of the Caspian Sea. It rapidly spread through Central Russia, and on the 18th of July, 1892, it again reached the populous market city of Nijni-Novgorod, where it met most favorable conditions for development and extension among travellers from all parts of Russia. It soon invaded St. Petersburg. In the month of August in the same year the disease appeared in Hamburg, but authorities differ as to its method of conveyance there. The river Elbe became infected, and the poorer inhabitants of the city, who drank this water unfiltered, were affected with the disease in large numbers.

Efforts were at first made by the local authorities to conceal the existence and extent of the epidemic, which only resulted in confusion and in danger to others.

From the foregoing brief account of recent epidemics of cholera it will be seen that there is a tendency of late years for the disease to recur in more frequent epidemics and to travel more rapidly and more widely than heretofore. This is unquestionably due to the extension of facilities for travel between the different countries involved and the enormous increase in the amount of commercial interchange. So long as India remained a comparatively isolated country the disease was kept for the most part within its borders, and when of late years it has extended throughout Europe and has penetrated to the United States, and even South America, its propagation has been due to emigration, for it is the poorer and more ignorant classes of the community, those who suffer most from inanition, overcrowding, and the consequences of infraction of all hygienic laws, who are the chief agents in conveying the disease in their persons and filthy clothing. In the last epidemic which reached New York, although 182 cases were brought over from Hamburg by several different steamships, they were confined entirely to emigrants, mainly the poorest of Russian exiles; the cabin passengers, who lived under better conditions, escaping entirely, although they were on the same ship.

ETIOLOGY.—*Predisposing Causes.*—The causes predisposing to cholera infection are those common to severe infectious diseases in general—namely, prevalence of famine, inanition, debauchery, chronic wasting diseases, over-exertion, either mental or physical, and alcoholism. In addition, it is believed that the individual is more liable to infection if the germs enter the alimentary canal during periods of indigestion or diarrhœa. While an epidemic prevails, therefore, it becomes exceedingly important to avoid the use of unwholesome food, such as decomposing meats, over-ripe fruit or vegetables, etc., and foul water.

Isolated cases of cholera may occur from time to time in remote regions into which the germs have been conveyed, but in general it is emphatically a disease of populous cities and camps and overcrowded localities where conditions of inanition and filth obtain. The infectious principle is not communicated by direct contact of one person with another, nor, as far as known, through the atmosphere, but is propagated solely by the stools of patients having the disease which have been allowed to contaminate clothing, transportation vehicles, baggage, or drinking water. It is often conveyed for long distances in overcrowded vessels and railway coaches.

Climate; Season of the Year.—Although it is well known that cholera is not propagated through the atmosphere, nevertheless, epidemics are favored by certain atmospheric conditions, especially warmth and moisture. The disease has been known to occur in every season and in every climate, with the exception of that of the Arctic regions, but its progress is usually checked by moderate cold, and, though isolated cases may occur during the winter season, epidemics do not prevail at that time.

Sex and *age* are two factors which exert comparatively little influence with cholera. Young children often acquire the disease, but it is not common after fifty-five or sixty years of age. Many cases occur among young adults, and males seem to be somewhat more susceptible to infection than females.

Race and Social Position.—All races are affected by the disease, and apparent difference in susceptibility can be traced more to general habits of life, personal cleanliness, religious observances in regard to bathing, etc., than to any inherent quality of the race itself. Owing to similar conditions the lower strata of society are very much more susceptible to the disease than those whose intelligence and circumstances enable them to secure better hygienic surroundings. The very poor, being subject to all manner of filth diseases and diseases of overcrowding, fall ready victims to the scourge of cholera.

During the fortnight from August 30 to September 15, 1892, seven steamships infected with cholera arrived at the New York Quarantine. For a few days longer the disease continued to spread while in port, and in all 128 suspects and patients ill with cholera were removed to the hospitals at Swinburne Island for treatment or to be held for observation. Of the suspects, all except 10 were subsequently proved by bacteriological examination to have the disease. There were many fatal cases which occurred, solely among the emigrants, while the vessels were at sea, and the fact that the majority originated either at the beginning or end of the voyage is probably to be accounted for as follows: The drinking water of the infected vessels was not found to contain the germs of the disease, for it had been steamed as a prophylactic measure; hence those cases which had developed immediately after leaving port were undoubtedly contracted upon shore, while those which developed at or near the end of the voyage must have been due to eating food which the emigrants of the class affected—the poorly fed and poorly clad—carried with them to supplement the ship's rations. This food, which consisted of such articles as sausage, bread, and cheese, they stowed in their bunks among their bedding and often wrapped up in soiled clothing. Being seasick during the early part of the voyage, which to most of them was an entirely novel experience, they did not resort to eating their own food until they had become somewhat accustomed to the sea, and thus were not infected until near the end of the voyage. The death-rate among these patients at sea was enormous, corresponding to the extreme malignancy of the disease at Hamburg, the port of departure of the vessels.

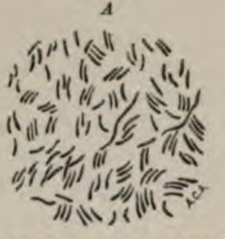
In August, 1893, 21 cases developed among steerage passengers quarantined at the hospitals in New York harbor, since which time no further cases have reached the United States, although the disease still prevails in Eastern countries.

THE COMMA BACILLUS.

That the comma bacillus, discovered by Koch in 1883, and so thoroughly described by him in his memorable address to the Berlin Cholera Conference, held on the 26th of July, 1884, has a direct causal connection with the production of Asiatic cholera cannot be doubted. All observers in all countries where this unwelcome visitor has made its appearance who have impartially studied this important problem of epidemiology are unanimous in accepting the comma bacillus as the pathogenic germ of this disease. That in some undoubted cases of cholera the most careful bacteriological examination has proved negative is also true. Such a result, however, depends upon the divers conditions of season and locality that belong to each individual case under examination. My own experience in three epidemics of Asiatic cholera (1884 to 1893) compels me, by the results of an overwhelming majority of examinations, to accept Koch's views regarding the causality of the comma bacillus as true. I have unquestionably met with cases in which all efforts to detect the presence of the specific germ by the ordinary methods proved fruitless, but the examination was made with material obtained either from advanced cases where the bacilli were eliminated or substituted by other germs, as often occurs, or it was obtained from small children, in whom it is extremely difficult to find the comma bacillus. In infants the cholera poison seems to act so violently that the last stages of the disease are reached before the germ has had time to propagate abundantly in the intestines.

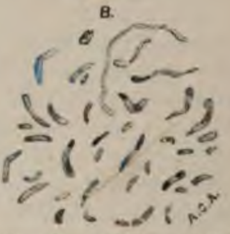
The comma bacillus of Koch is a spirillum presenting a curved form, which sometimes appears like a comma, and again as a crescent or a double curve like an S. The bacillus is short, measuring not more than .5μ to 1μ, and it is somewhat broader than the tubercle bacillus. The germ grows rapidly upon a variety of culture media when subjected to very moderate moisture. It has been found thus growing upon potatoes and other raw vegetables, befouled clothing, and damp earth. According to Sternberg, it is easily destroyed by a temperature of 140° F., but it survives freezing to even 10° C., its activity being only temporarily suspended thereby. It is also suspended by a moderate acid medium, and the germ is destroyed by strong acids. For this reason it is not developed in the stomach, and hence the desirability of preventing dyspepsia and an alkaline reaction of the stomach during the prevalence of cholera epidemics.

FIG. 32.



Spirillum of Asiatic cholera. Impression cover-slip from a colony thirty-four hours old (Abbott).

FIG. 33.



Involution forms of the spirillum of Asiatic cholera, as seen in old cultures (Abbott).

The germ often presents one or two cilia at one extremity, which give it active motion. It is among the most active of germs in reproduction, which is accomplished by direct fission and not through the intervention of spores. The germ flourishes and propagates rapidly in foul and brackish water, and hence it is in almost constant prevalence along the delta of the Ganges (Koch). The researches of Klein and Gibbes, conducted in India for the British government, demonstrated the existence of several other species of bacilli which present slight morphological differences from the cholera bacillus, but which produce somewhat analogous symptoms in the lower animals; but there is no difficulty in isolating the comma bacillus, even when associated with other forms, when the proper methods of culture before described are closely followed.

The individual germ does not appear to be very long lived, but it propagates with such rapidity that the species is easily perpetuated. Exposure to drying and sunlight is fatal to it in a short time. Koch has proved conclusively that the spirillum is promptly destroyed by drying or exposure to dry air. In a thin film of fluid containing the germs they do not survive more than three hours when dried in the atmosphere. Sternberg tested small squares of sterilized blanket which he moistened with a bouillon culture of the spirillum and then exposed to strong sunlight. Four hours sufficed to render the germs inactive. The prevalence of cholera epidemics has been very largely checked in many instances by draining salt marshes and placing the soil in better condition. The germ undergoes a curious change outside of the body in regard to air. Within the body, its habitat being the intestine, it is necessarily anaërobic, but after the evacuated germs have been out of the body for some time they become distinctly aërobic, and so behave in regard to culture media; hence when artificially cultivated in an alkaline fluid medium they form surface colonies. This fact points to the desirability of the prompt disinfection of cholera stools before the germs have had time to change their character.

The germs grow rapidly in peptone solution, forming large cultures in six hours or less.

For a long time it was believed that the lower animals were immune to cholera—at least, that they could not be saturated with the disease—but the researches of Koch and Pasteur, conducted on dogs and guinea-pigs, have demonstrated that these animals at least may harbor the cholera bacilli, and be affected by symptoms closely resembling genuine cholera.

In the human body the germs are found only in the alimentary canal, principally upon the surface and within the open tubules of the mucous glands of the ileum.

Method of Examination of the Stools for Bacilli.—During the month of August, 1893, I had the opportunity of treating 21 cases of cholera at the Quarantine Hospital on Swinburne Island in New York harbor. This outbreak of the disease took place among the five hundred steerage passengers of the steamship Karamania after her arrival in quarantine on August 3, 1893. The vessel sailed from Naples, which was at that time an infected port, and during the Transatlantic voyage four or five fatal cases of "gastro-enteritis" were reported by the ship's surgeon, although the drinking water on board was uncontaminated by the spirillum of Asiatic cholera.

In each of my cases, with but a single exception, that of a young child, the comma bacillus was found. This child presented an undoubted case of cholera, although no comma bacilli were present in the stools. The child was subject to infection, and had both the premonitory and secondary symptoms of the disease in a most typical degree;

but, as above stated, there are instances among children in which a most conscientious and painstaking bacteriological examination fails to demonstrate the commas.

The method used by me at Swinburne Island for the bacteriological diagnosis of Asiatic cholera was the following: As soon as the patient arrived at the hospital an enema of sterilized lukewarm water was given. By this means material for examination was obtained almost immediately, thus avoiding delays in the treatment and the bacteriological examination, as is the case when a spontaneous stool is awaited. The material voided was collected in sterilized tubes and taken to the laboratory and cover-glass preparations were made and stained. In the mean time tubes containing Dunham's solution of gelatin and agar were seminated with the suspicious material. The details of these examinations follow:

1. *Microscopical examination of the dejecta* is easily performed, but is valuable only as a positive test. In very many instances I have found the result either negative or uncertain, and the typical grouping of the bacilli described by Koch was rarely observed. The method employed was quite simple: a cover-glass preparation was made and stained with a dilute Ziehl's solution of carbolic fuchsin.

2. *Cultures* were implanted in the following media:

    (1) Tubes of peptone salt solution in the proportion of peptone 15, sodium chloride 5, distilled water 1000.

    (2) Gelatin tubes prepared by addition of 10 per cent. gelatin to the above peptone solution (1).

    (3) Agar-agar tubes, prepared by addition of 1 per cent. agar-agar to the peptone solution (1).

Precaution must be exercised to maintain a distinctly alkaline reaction in all culture media employed, for gelatin especially is liable to alter in reaction, and it may become neutral or slightly acid—an occurrence which is fatal to the growth of the germ—or else it so modifies it as to render a diagnosis impossible. In my experience a strongly alkaline reaction is more favorable for the growth of the germs than the faintly alkaline reaction generally employed in laboratories.

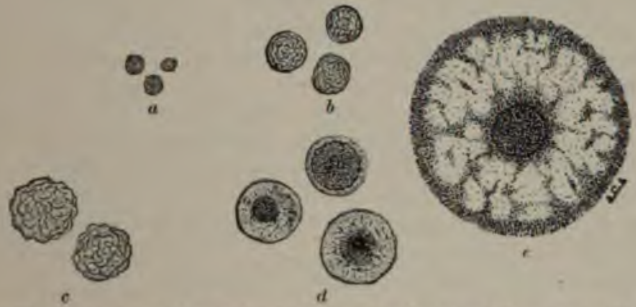
(1) The peptone tubes were immediately placed in an incubator at a temperature of 37° C., and from the gelatin cultures in Petri dishes were made. The former were kept at a temperature of 22° C. and the latter at 37° C. in the incubator. Each tube or plate was regularly examined at intervals of three or four hours, and the conditions of growth were noted. Over 200 examinations were made from the 21 patients kept in the hospital, both during life and *post-mortem* in the fatal cases. Furthermore, as soon as a vestige of growth appeared in the peptone solution tubes, which invariably takes place after a few hours (four to eight), a new series of gelatin plate cultures was made as a control.

Dunham's culture method is a modification of that practised by Schotellius, which is to be strongly recommended. A wide test-tube is filled with a sterilized solution consisting of peptone 1, sodium chloride 0.5, water 100. Into this mixture is dropped a small quantity of fæces or a flake of mucus from a rice-water stool, and the tube is then placed in an incubator at 37° C. for from six to twelve hours, when the germs, if present, will be found floating in almost pure culture upon the surface, from which in time cover-glass preparations and gelatin roll cultures are made.

(2) *Gelatin Roll Cultures.*—Esmarch's modification of Koch's method gives very satisfactory results. Rapid cultures are made after Dunham's method described above (1), and the bouillon gelatin is rolled after transplantation with a drop from the cultures. The tubes are kept at 20° C., and are examined after from twelve to twenty-four hours.

There are certain characteristics regarding the individual form of the bacilli, the appearance of the colonies on gelatin and agar plates, and the property of absorbing color by the bacteria, which should be emphasized, as in some cases they may be confusing to an observer of limited experience. The direct examination of the dejecta is not to be relied upon. Some authors advance the opinion that a diagnosis can be made by this means. Such would be the fact if in every case we met with the characteristic disposition in swarms of well developed comma bacilli as described by Koch, but this seldom happens. It is astonishing that fæces, which under culture yield only pure colonies of comma bacilli, when examined microscopically present a great variety of bacteria, among which the commas are in the minority or are not at all to be found. We cannot, and should not, rely at all upon such examination, especially when upon the diagnosis depends the welfare of the community. A thorough bacteriological analysis requires but a few hours and then a positive diagnosis can be given.

FIG. 34.



Developmental stages of colonies of the spirillum of Asiatic cholera at 20° to 22° C. on gelatin. × about 75 diameters: *a*, after sixteen to eighteen hours; *b*, after twenty-four to twenty-six hours; *c*, after thirty-eight to forty hours; *d*, after forty-eight to fifty hours; *e*, after sixty-four to seventy hours (Abbott).

The comma bacillus presents some peculiarities in form and grouping which are noticeable. Cunningham described a series of transformations in this germ which other authors have contradicted, but it is a fact that such modifications do occur, and that the modified characters are present in succeeding generations. In 1892 all the cultures obtained, using identical media, gave rise to a very delicate, long, slender comma bacillus, which I still keep in the laboratory. This race of comma bacilli can be actually differentiated from the bacillus of 1893. But even during the same epidemic a difference can be noticed in the individual morphology of some cultures. This does not include the modifications induced either by a change of reaction of the media or change of the temperature in which the germs live, nor the age of the culture. I refer simply to such forms as are obtained *d'emblée*, and which continue to grow with the same characteristics. In 1893 a very striking example of such variations was given by three cases, each of which gave rise to an abundant growth within thirty-six hours in the peptone solution of exceedingly well-defined spirilla, while in the rest of the cases several days (ten to twenty) passed before these forms appeared.

The temperature and the reaction of the media are also factors influencing the individual appearance of the germs. Gelatin cultures kept at the ordinary temperature of 22° C. constantly produced well defined curved rods. If the temperature is lowered, the curvature in each individual germ is much more evident. Contrary to this, bouillon and agar cultures kept in the incubator at 37° to 38° C. present short, stumpy, straight rods, which greatly resemble at times the colon bacillus in appearance.

Colonies obtained in plate or tube cultures also vary, and should be duly studied by the sanitarian, as their appearance may lead to regrettable errors. I refer only to young colonies in gelatin when liquefaction has not taken place. I have observed at least five well defined varieties of colonies either occurring contemporaneously in a plate or separately in different plates. These are—

1. Colonies almost transparent, finely granular, with a well defined circular edge.

2. Colonies small, yellowish, thick, coarsely granular, circular, with jagged or undulated edges, which appear like little heaps of ground glass. These are the classical colonies described by Koch.

3. Colonies of elliptical shape, very finely granular, dark brown, non-transparent, with well defined edges of a lighter hue.

4. Colonies round, light yellow, with granular centres surrounded by a dark circular edge.

5. Colonies round, dark, with coarsely granular centres surrounded by a yellowish ring with wavy edges, from which irradiations are sent into the surrounding gelatin.

After the gelatin begins to melt all these colonies gradually lose their characters, giving rise to the well known funnel-shaped depressions on the gelatin, at the bottom of which lie the colonies surrounded by the melted gelatin.

On agar plates kept at brooding temperature I have observed but two varieties of colonies—the deep ones, which appear under the microscope as small dark, round, or elliptical, coarsely granular dots, and the superficial ones, appearing as large, thin, yellowish, irregular growths with wavy, finely granular edges, very much resembling some colonies of the colon bacillus.

Cultures in peptone solution rendered strongly alkaline and kept at 37° C. present in a few hours a pellicle floating on the surface, whereas in slightly alkaline solutions the pellicle does not form or takes several days to form, especially if the colon bacilli are present in superior numbers.

The reaction to coloring solutions, such as diluted Ziehl's carbolic fuchsin, differs somewhat according to the media in which the bacilli grow and the temperature at which they are cultivated. Cover-glass preparations made from bouillon cultures do not stain as well as those from gelatin cultures. The bacilli absorb the dye irregularly, presenting here and there vacuoles which might be mistaken for spores.

Although stained specimens of dejecta present a variety of bacteria in cultures, I found but two other germs which were associated with the comma bacillus. In all cases excepting three the comma was associated with the colon bacillus in pure cultures, and in two cases comma bacillus, colon bacillus, and proteus vulgaris were associated. It should be noticed that in the first diarrhœal discharges the colon bacillus is more abundant than the commas, whereas during the prevalence of rice-water discharges the commas are in the majority; and then, again, the colon bacillus begins to increase as the disease advances.

The indol reaction was tested in every case by adding a few drops of c. p. sulphuric acid to a peptone solution kept in the incubator for twenty-four hours. The acid reaction prevented differences in the hue. I have also obtained quite an evident indol reaction by adding to the diluted and filtered rice-water dejections a few drops of sulphuric acid. Lately I have observed that by adding a few drops of a 1 : 10,000 aqueous solution of nitrate of potash the indol reaction appears with greater intensity.

PATHOLGICAL ANATOMY.—The lesions produced by the cholera infection, although the localization of the germ in the intestines is well established, are so far from being constant that but little can be obtained from an autopsy to aid the diagnosis. These lesions, which from time to time occur, bear little or no definite relation to the intensity of the symptoms. A disease which may terminate fatally in three or four hours from its onset gives no time for extensive pathological lesions to develop. Visceral congestions and hemorrhages, with great emaciation and dryness of the tissues, are perhaps the most characteristic findings.

Rigor mortis is present early and is well marked, but I have failed to note the unusual positions of the body described by some pathologists. There may be slight contractures of the flexor muscles of the hands and arms, but there is nothing unwonted in that.

The *skin* becomes actually warmer than during life, owing to the cessation of previous excessive perspiration. It is pale and wrinkled, and the purple hue of asphyxia is absent, excepting perhaps on the cheeks and backs of the hands.

The *eyeballs* are deeply sunken, the orbital fat has disappeared, and the eyes have a lack-lustre look beyond that of the ordinary cadaver.

Putrefaction sets in very slowly, even in hot weather. This is probably due to the fact that so much water has been drained from the tissues.

The *brain* itself appears normal, but the ventricles are dry and viscid; so also is the surface of the pia mater. The meningeal vessels are injected.

The *heart* is dark; the left ventricle alone is in systole, the other chambers being usually dilated and filled with dark, fluid, viscid blood. I have observed cardiac thrombosis. The pericardium is usually dry, but it may contain a little serum. Sometimes numerous hemorrhages, varying in size from a pinhead to an inch in diameter, are found on the surface and in the parenchyma of the heart. The aorta is filled with fluid blood.

The *lungs* are highly congested, of a dark purple hue, and œdematous. In some cases lobar pneumonia is found. In others numerous hemorrhages, varying in size like those in the heart, are present all over the pulmonary surfaces and in the parenchyma. The pleuræ are dry, coated with viscid fluid.

The *peritoneum* is dry and resembles ground glass. It is coated, like the other serous membranes, with glairy, viscid fluid.

The *liver* is sometimes small, and light yellow in color, or it may be of a dark purple hue or present hemorrhagic spots. I have observed perihepatitis. The gall bladder is usually distended with viscid yellowish mucous fluid, from which cultures of comma bacilli are obtainable.

The *spleen* is of normal size, somewhat hard and purple or hemorrhagic. There is sometimes perisplenitis.

The *stomach* appears small, with venous congestion in the larger vessels, but the mucous membrane is usually normal and covered with a thick, tenacious layer of creamy mucus. Sometimes the natural folds of the mucosa are much exaggerated by contraction, and exhibit congestion and punctate hemorrhage.

The *kidneys* are sometimes normal, sometimes large and yellowish, but if the disease has lasted for several days they usually present the appearance of acute parenchymatous nephritis. The so-called "cholera kidney" does not differ from that of all severe acute infectious diseases, and is therefore not diagnostic. The bladder may be distended with albuminous urine, but in the majority of cases it is contracted and empty.

None of the above described lesions are constant or characteristic, nor are they all observed in any one case. When present they bear no definite relation to the intensity of the symptoms. In children in general the lesions are all less distinct.

The Intestines.—At times the intestinal tract is found normal, but profound lesions are discovered in many cases.

The *small intestine* is contracted, and presents venous and capillary congestion, particularly in the ileum. The contents may be copious, rice-water exudation or viscid greenish-yellow mucus tenaciously adhering to a normal or hemorrhagic mucous membrane. Both the solitary and agminated glands are considerably enlarged.

The *mucous membrane* is often found denuded of epithelium where the germs have been most active, the follicles being choked with granular and epithelial débris and masses of bacilli. The germs are also found in the subepithelial layer of the intestinal mucosa, into which they penetrate by their own motion.

The Large Intestine.—The contents of the large intestine consists of large quantities of rice-water fluid, excepting after intestinal irrigation, when creamy, tenacious, or blood-stained mucus is found clinging to the mucosa.

A lesion with which I have constantly met, and which I think is of great diagnostic importance, is the condition of the large intestine. It seems that the cholera poison formed in the small intestine passes into the large intestine, where absorption takes place, giving rise at the same time to inflammatory symptoms which I have never found absent in these autopsies. The condition of the large intestine is that of dysentery; the mucous membrane is swollen, and presents here and there large patches of gangrene or hemorrhages which at times involve all the coats of the gut. Cruveilhier was the first to call attention to the importance of this condition during the last epidemic of cholera in Europe.

Identical observations are reported by Guttman,[1] Fürbringer,[2] Kirchner,[3] Ceci and Klebs,[4] and others. We should, however, acknowledge that we are far from knowing the biological changes that take place in the diseased intestine in the different stages of Asiatic cholera, and the influence such changes may have upon the vitality of the comma bacillus. In fact, it is a matter of common occurrence to find few commas during the prodromic stage, whereas they are present in almost pure cultures in the evacuating stage, and again disappear or are rarely found in the typhoid stage.

Although no anatomical lesion is pathognomonic of cholera, if the series of lesions above mentioned are observed in a suspected case where no other cause of death can be discovered, then one is justified in making at least a conditional diagnosis of Asiatic cholera.

The following report of an autopsy which I performed ten hours after death gives a fair idea of the lesions of a typical case:

AUTOPSY.—Female, aged thirty years.

Appearance of Body.—Moderately emaciated; rigor mortis well marked; features pinched.

Thorax.—A few pleuritic adhesions, indicating a previous plastic pleurisy. The right pleura presents evidences of an acute pleurisy; left pleura normal. Lungs emphysematous in their antero-lateral surface; both lungs present extensive areas of broncho-pneumonia in the upper lobes; inferior lobes hypostatic pneumonia and œdema, also punctiform hemorrhages throughout the parenchyma and subpleural space. Large bronchi and trachea very much congested. Pericardial sac contains about two drachms of thick, creamy pus and other evidences of acute prevalent pericarditis. The heart, normal in volume, presents the left ventricle in systole, the other cavities filled with dark fluid blood; valves normal and competent. Aorta normal.

Abdomen.—All organs in proper relation. Upper surface of liver covered by recent fibrous exudation; the rest of peritoneum appears dry, and of a peculiar "ground-glass" hue. Liver of normal volume; upon section presents a slight nutmeg and fatty appearance; gall bladder filled by a mixture of bile and mucus; spleen small and consistence increased; kidneys large and yellowish; on section present the signs of acute parenchymatous nephritis, also slight chronic interstitial nephritis. Suprarenal capsules normal.

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[1] "Tödtlicher Ablauf eines Falles von Cholera nostras," *Berl. klin. Woch.*, 1892.

[2] "Tödtlicher Cholera verdachtiger Fall in Krankenhause Fredrichshain," *Deutsch. med. Woch.*, 1892.

[3] "Bacteriologische Untersuchungen bei Cholera nostras und Cholera Asiatica," *Berl. klin. Woch.*, 1892.

[4] "Ueber Cholera Asiatica nach Beobachtungen in Cenna," *Correspondenzbl. f. Schweizer Aerzte*, 1884.

Alimentary Canal.—Stomach normal in dimensions; on section its mucous membrane is seen covered by a thick, creamy deposit of mucus, underlying which can be noted extensive and intense hyperæmia, with large patches of extravasated blood. These hemorrhages are specially noticeable in the fundus and pylorus; the duodenum and rest of the small intestines present evidences here and there of acute enteritis. There are hemorrhagic areas, principally in the lower portions of the ileum. Large intestine from cæcum to descending colon very much congested, and at intervals hemorrhagic. Intestinal surface (large and small) presents the characteristic staining due to tannic acid (from enteroclysis), and the contents are fluid and of a brownish color.

Pelvic Organs.—Ovaries normal. Bladder empty. Rectum presents the signs of acute proctitis. Uterus pregnant; contains a female fœtus about twenty-eight weeks old, well nourished, on which an autopsy was performed, and all organs found apparently in normal condition except the bladder, which was enormously distended with urine.

Adipose tissue very scanty; muscles of a dark reddish color; dry.

Diagnosis of Asiatic cholera confirmed by bacteriological cultures.

SYMPTOMS.—The symptoms of cholera are exceeding acute, typical, and constant. They are produced, it is believed, on the one hand, by the absorption of toxic material and its effect on the system, and, upon the other hand, by the rapid and unwonted drainage of fluid from the blood and lymphatic vessels. It is not easy, however, to differentiate clinically the various symptoms in relation to the special cause which has produced them, and, although a matter of considerable scientific interest, it is of no practical importance to do so. For purposes of clinical description it is convenient to subdivide the course of the disease into four stages, which merge into one another, however, without decided demarcation. These stages are as follows:

I. Premonitory stage;
II. Stage of serous diarrhœa;
III. Stage of asphyxia and collapse, known also as the algid stage;
IV. Reaction.

The first stage is occasionally omitted, especially in the more severe epidemics, when persons are attacked with great suddenness and violence by the disease. Many patients die in the third stage without ever reaching the fourth. Very mild cases may occur in connection with an epidemic, especially at the commencement and end of it, in which the third stage, or even the second stage, is absent. In some cases, although they are in the decided minority, there is an undefined prodromal stage of a day or two, during which the patient complains of malaise, exhaustion, loss of appetite, and flatulent dyspepsia, with possibly vertigo.

I. The PREMONITORY STAGE is characterized by more or less lassitude and diarrhœa, which, at first mild, soon increases, the stools becoming more and more frequent, watery, and abundant. They are usually passed without pain, are alkaline in reaction, and have a pale yellowish color. They may occur as often as once every two hours, even once an hour. There are more or less intestinal indigestion, frequent vomiting, and considerable flatulence. There is headache and the patient is nervous, and, if aware of the prevalence of an epidemic, is apt to be filled with fear and apprehension. The tongue is not coated, but is pale, thin, and moist. It soon becomes dry, however, and thirst is early complained of, which afterward becomes excessive. The voice is usually faint and the patient experiences great muscular languor. Excepting the headache there is no decided pain anywhere. The expression becomes unnatural, evidencing dread, and the complexion is pallid. The pulse may be slightly quickened, but there is nothing distinctive in the character of either pulse, respiration, or temperature in this stage.

The premonitory stage may last for one or two days, and if promptly treated may end in immediate recovery. Otherwise it will merge into the second stage of serous diarrhœa, and, as stated before, it may be abbreviated even to a few hours or it may be absent altogether.

II. The SECOND STAGE presents one of the most alarming conditions ever recognized in any of the infectious diseases, excepting, perhaps, yellow fever. The stools become more and more frequent, finally almost continuous. They are still alkaline, and they become more and more watery until they finally consist only of water, in which flakes of whitish mucus and epithelium float about, giving rise to the characteristic appearance familiarly known as "rice water." The bowels having been thoroughly evacuated of all fecal matter and bile by previous passages, the stools become purely sero-mucous and odorless, though there is a distinct meaty smell. They are frothy and exceedingly copious; as much as two quarts of fluid may be almost instantaneously evacuated with considerable force. If left standing, a sediment is deposited which, when examined, is found to consist principally of desquamated intestinal epithelium, granular débris, bacteria, and possibly a little mucus. The stools, although described as resembling rice water, are in reality much more transparent (Milles). In some cases they are stained with blood pigment, and, according to Flint, the specific gravity of the evacuation is 1005 to 1013. They contain sodium chloride and also ammonium carbonate, which latter imparts the alkaline reaction. There is at first a notable absence of tormina and tenesmus; in fact, patients are often temporarily relieved by the evacuations. When the stools become typical they are found to contain fewer varieties of bacteria than are present normally, and, in fact, the comma bacillus may be the only one present. This germ, however, is not found in any considerable quantity until the evacuations are thoroughly watery.

The quantity of fluid drained from the system by this means is enormous, and far exceeds that which is ingested. It should be remembered that about 70 per cent. of the normal body weight is composed of water, and while the evacuations continue much of this water is drained from the more fluid tissues, such as the muscles and viscera, and is withheld from the digestive organs, and is reabsorbed from the serous surfaces. Hence all the latter become dry or coated with a sticky, thick, slimy secretion, and the soft tissues generally diminish in volume. Brunton considers the transudation of serum into the intestine as due to paralysis of the intestinal nerves. The facies are typical in this stage. The rapid emaciation, showing prominently in the face, gives the individual a wizened aspect. The conjunctivæ are red and congested, the pupils are contracted, and the orbits are hollow and are generally surrounded by dusky rings. The eyes have a vacant, staring, cadaveric, expressionless look. The face is flushed, the nose is pinched, the mouth is drawn, the cheeks are sunken, the abdomen is depressed and "boat-shaped," the skin becomes inelastic, loose, and wrinkled, and the muscles lose in volume. A few hours will make a previously healthy-looking young adult appear like a withered octogenarian.

The tongue is dry, covered with a thick, yellowish white coat in the centre, but red at the edges and tip, somewhat resembling the tongue of typhoid fever, but with less prominent papillæ. The whole mouth is very dry and thirst is extreme. The desire for fresh water and for acidulated drinks is insatiable. Patients drink eagerly, and never seem to get enough water. Among other subjective sensations complained of are headache and a feeling of oppression or of suffocation in the chest. Restlessness gives way to quiet and apathy.

The mental condition of the patient is characteristic. The mind is dull, listless, apathetic, but consciousness may remain until death supervenes, and the patient can often be aroused to answer questions intelligently, although he volunteers nothing, but moans and rests with the eyes half closed. When aroused from this semi-conscious condition the voice is feeble, cerebration is slow, and speech is difficult. If asked how he feels, the patient may reply that he is well, but asks at once for more water.

Vomiting usually characterizes this stage, and it comes on suddenly or is preceded by nausea. It is difficult to control, and is often accompanied by considerable straining and consequent epigastric pain and soreness. The stomach is at first emptied of whatever food it may contain; then bile is vomited, and finally the ejecta consist of watery fluid, become colorless, almost odorless, alkaline in reaction, and resemble the choleraic stools. The urine, like the other secretions in the body, is withheld, and suppression may become complete, or, if this is not the case, it is dark-colored, of high specific gravity, containing an excessive percentage of urea, some albumin, and hyaline, granular, and fatty casts.

The anuria is not wholly due to lack of water in the blood, but in great part to inability of the kidneys to perform their functions. The scrotum is retracted. The pulse, owing to the small volume of blood contained in the arteries and the feeble heart action, becomes very thread-like and compressible. It is quickened, at first to 100, later it may rise to 115 or 120. Arterial tension is diminished. The respiration becomes feeble and shallow. It is mainly thoracic, and may be irregular in rhythm. It may be increased to 30 or 40. The perspiration is often profuse, being the only secretion which is not checked. The surface of the body becomes livid, and feels cold and cadaveric to the touch, although the internal temperature may register one or two degrees above the normal when carefully taken by a long-stemmed thermometer placed in the rectum. It is often stated that cholera is a disease of subnormal temperature, but this is not strictly correct, as pointed out by De Renzi, Guterbock, and others. Although the temperature in the mouth has been recorded as low as 79° F. and that in the axilla at 75° F., the internal temperature is elevated, and the patient complains of a subjective sensation of fever. The fever is described as being of a remittent type with exacerbations. This temperature is commonly overlooked on account of the frequency of the stools and the difficulty of taking the temperature correctly in any other place than the rectum. The freshly voided urine may show an elevation of temperature. The muscular cramps may affect the diaphragm, giving rise to more and more difficult respiration, or, occurring spasmodically, cause hiccough.

The stage of serous diarrhœa lasts from one to two or three hours or more, and the patient usually passes into the stage of collapse. More rarely recovery takes place at the end of the second stage. Naturally, the more violent the symptoms of this stage the briefer it becomes.

One important fact should be borne in mind—namely, that the quantity of the evacuations is not an infallible guide for prognosis. A very fatal form of cholera is sometimes observed in which diarrhœa is slight, although the other symptoms are all present. This is described as "dry cholera," or "cholera sicca." Such are often cases in which the patient is suddenly seized with great prostration and faintness without any premonitory symptoms. Death occurs in two or three hours, and examination of the intestines shows them to be enormously distended with serous fluid which failed to escape in diarrhœal stools, apparently because intestinal paralysis has been complete.

THE STAGE OF COLLAPSE cannot be distinctly separated from the stage of serous diarrhœa, for they gradually merge one into the other. In this algid stage the heart action becomes so feeble on account of the lack of blood pressure, the difficulty of propelling the thickened blood through the capillaries, and the lack of nutrition of the organ itself, that stimulation is urgently needed.

Owing to the excessive loss of water by osmosis into the intestine the blood becomes thick and tarry. The bloodvessels are comparatively empty, and the velocity of the blood stream is reduced by the weakness of the heart. The red corpuscles do not circulate readily through the pulmonary capillaries, and the normal respiratory function is greatly impeded. There is deficient oxidation, and carbonic acid accumulates in the blood. Cyanosis results, and this becomes especially marked about the nose, lips, and in the extremities.

As a further consequence of the rapid loss of fluid from the system the muscles become dry and pass into tonic spasms, in which they are hard and board-like. Severe and frequent cramps ensue in them. The abdominal recti are usually first affected, and subsequently the calves of the legs, and finally nearly all the larger muscles of the extremities and trunk, may be involved, including those of the arms and neck. The cramps are persistent, and give rise to intense, agonizing pain, especially in the abdomen and legs. The arms and legs are distorted. Pain is also referred to the sternum and other parts of the chest.

The patient's general condition is pitiful. The skin is dry, pinched, and wrinkled, the face is expressionless, the half-closed eyes have a vacant stare; the mouth is drawn and set; the cheek-bones protrude as if they would burst through the skin; there is sudden increase in vomiting and diarrhœa, which is followed by further fall in the surface temperature (Shakespeare), although the deep internal temperature may continue elevated by one or two degrees. The patient's mouth is so dry and he is so feeble that he is unable to articulate, although he can be aroused to evident consciousness. The muscular cramps continue, and the abdominal walls are sunken, but rigid. The emaciated fingers and toes are flexed or drawn into unusual positions by the contractures. The respirations become more and more feeble and irregular, and the exhaled breath is cold. The patient often suffers greatly from a sense of suffocation. The tears, saliva, and bile are all suppressed, and so is the menstrual function. The conjunctivæ become so dry that exposure to the air may make them inflamed (Stillé). The urine continues highly albuminous or else is totally suppressed. It sometimes contains sugar. The rapidity of the pulse is not excessive. It often remains between 100 and 120, and it finally becomes imperceptible at the wrist. The second sound of the heart is quite inaudible. The duration of this stage varies from a few hours to as much as one or two days, ending either in the stage of reaction or in a typhoid state in which the patient may linger for a week or more before death, or, as is frequently the case, it terminates early and the patient dies of asthenia. Death sometimes occurs from sudden heart failure, and the patients who have not presented the most severe symptoms have been known to escape from bed, take a few steps, and drop dead. Usually, however, death occurs so gradually that it may be difficult to fix the exact moment at which the heart action finally ceases. Just before death and for some time thereafter the temperature begins to rise, and within an hour or two after death it may reach 106° F. In the asphyxiated cases, caused by stagnation in the flow of the thickened blood, the temperature may even reach as high as 108° F. Not infrequently rigor mortis sets in while the patient's facial muscles and those of the extremities are so contracted as to produce fixed grimaces and contortions, which add much to the horror of the disease.

IV. STAGE OF REACTION.—This stage follows gradually upon that of collapse. The diarrhœa and vomiting, which have ceased toward the end of the previous stage, either from exhaustion or from lack of fluid to be voided, do not return. By slow degrees the pulse becomes again perceptible, and the internal temperature begins to rise, in the majority of cases for two or three or more degrees. The patient's expression becomes more intelligent, and muscular contractures cease. The respiration becomes deeper and more regular, and slowly the external warmth of the body is restored. The patient ceases to experience thirst, and there is gradual evidence of the recovery of the different secretory functions which have been suppressed. The urine increases in volume and improves in character, and the stools, which are now infrequent, by slow degrees take on a solid character (after nourishment has been given), and show some evidence of bile pigmentation, although if there has been excessive denuding of the epithelial surface of the intestine they may continue to have a hemorrhagic character.

Recovery is sometimes prompt, but, as might be expected from such a severe disease, it is often protracted by continued anæmia and pronounced irritability and feebleness of the stomach, bowels, and nervous system in general. Such symptoms as severe frontal headache, dizziness, and fainting may recur from time to time. In other cases septic material is apparently absorbed from the denuded intestinal surfaces, and the patient passes into a condition of septicæmia or a typhoid state, in which he may linger for a week or two before death. This condition is characterized by continued high fever (104° to 105° F.), a dry fissured tongue, continued diarrhœa, delirium, and coma. Sometimes there are cutaneous eruptions of different kinds, having no constant type, however. Other cases, again, owing to the continued suppression of urine, pass into a uræmic condition, with a preponderance of nervous symptoms, such as delirium and convulsions. In still other cases the intestines have been so much weakened that they are long in regaining their natural tone, and protracted diarrhœa maintains the exhaustion of the patient. Relapses sometimes result from overexertion, too hasty resumption of normal diet, or occasionally without any assignable cause.

In the disease called "cholerine," which has been mentioned as often preceding or accompanying widespread epidemics of cholera, and which some writers regard as a mild form of the latter disease, the symptoms are much less severe, and, although the diarrhœa is exhaustive, asphyxia, muscular cramps, and total suppression of the urine are not common. This disease, however, is often fatal.

DURATION.—The cases which are fatal commonly terminate in two or three days. Death has been known to take place within two hours after the passage of the first typical stools, the patient going into the algid state at once. Ordinary cases, ending in recovery, may last from a week to several weeks according to the severity of the disease and the supervention of complications. Epidemics do not long prevail in any one locality. They do not often remain longer than three or four weeks in one place, but, being migratory, pass on to new localities, and are thus sometimes prolonged throughout an entire season. They may be temporarily checked by cold weather and be resumed in the spring.

COMPLICATIONS AND SEQUELÆ.—Owing to the conditions under which cholera develops, especially those of the presence of a damp soil, putrefying organic material, and bad water, other diseases are apt to prevail in the same locality and at the same time in which cholera is active. Such diseases are simple diarrhœa, gastro-enteritis, dysentery, and the more severe forms of malarial fevers.

A variety of symptoms have been recorded in different epidemics as complicating or following cholera, but none of them are distinctive or constant. Such are the different exanthemata, as roseola, urticaria, etc. The emaciation predisposes to bedsores, ulceration, and furunculosis. Perspiration may continue and become excessive, the sweat containing urea. Painful swelling of the parotid glands has been recorded. Occasionally a condition resembling tetanus obtains, and the muscles remain rigid and contracted for several days. Still rarer sequelæ are gangrene, peritonitis, and ulcer of the cornea. Very commonly considerable irritation of the gastro-intestinal tract persists after many days or weeks, which naturally postpones convalescence. The circulation may remain feeble for a long time, so that the patient suffers from coldness of the extremities, wakefulness, dizziness, and other symptoms. Persistent albuminuria may remain, and there is sometimes cerebral congestion. In many cases, and in children especially, broncho-pneumonia is a somewhat common complication.

DIAGNOSIS.—The immense importance of an early diagnosis of Asiatic cholera is self-evident, for not only is the clinician materially aided by being thus enabled to apply the proper treatment at the onset, but the sanitarian can more easily control an impending epidemic by prompt recognition of the first cases. The diagnosis is, however, beset with difficulties even during the prevalence of an epidemic, for, on the one hand, a number of very mild cases escape detection—which for this reason are apt to spread the scourge in its worst form—and, on the other, there are undoubtedly many cases of severe acute gastro-intestinal disease which so closely simulate Asiatic cholera as to be neither clinically nor anatomically distinguishable from it. These cases are due to other bacteria than the comma bacillus, which are endowed with either permanent or temporary specific virulence. Fortunately, in the recognition of the spirillum of Asiatic cholera discovered by Koch we have a means of diagnosis which is today admitted by the great majority of authorities to be absolute. Hence in all suspected cases early bacteriological examination is imperative, and whenever the spirillum is found the case is at once to be regarded as one of true Asiatic cholera. Upon the negative side it must be admitted that there are cases of true cholera in which the spirillum cannot be found, but these are far fewer of late years since the bacteriological technique has made such rapid advances and the examinations are made more promptly. The causes of failure to find the bacillus in such cases are chiefly the following: 1. Imperfect technique. 2. Examination conducted after the intestines have been already irrigated with acid injections. 3. Examination made at the wrong stage of the disease, when the bacilli are absent or greatly reduced in number. 4. Some few extremely virulent cases, occurring especially in young children, in which death results before there has been time for the development of many germs.

The panic caused by Asiatic cholera, no matter in what community or class of people it may appear, is only to be judged by those who have an opportunity of being witness to such scenes. The most formidable barrier the sanitarian meets with in his endeavors to check an epidemic is the fear possessed by the masses. People imagine that the authorities are hunting for the sick, not to help them in their distress, but to exterminate them by any means. When a patient is taken to a lazaretto his relatives and friends are often convinced that he will be poisoned at once and hurried into an unknown grave. Consequently in hospitals one very seldom sees cases of cholera in the first stages of the disease. This experience was repeated during my stay in the New York Quarantine in 1892 and 1893.

There are three symptoms which are present at the outset of the disease, the observation of which has aided me and others connected with the quarantine in diagnosing suspected cases at a very early stage. These symptoms are as follows:

1. *Expression of the face.* The face appears pale, with slightly flushed cheeks, a bluish hue of the lips, slight congestion of the conjunctivæ, and a peculiar, rather stupid look in the eyes.

2. *Moderate rapidity of the pulse.* This symptom is most important, and is one of the earliest to appear. The pulse is compressible, and beats about 108 to 120 a minute without accompanying elevation of temperature.

3. *Appearance of the tongue.* This is thickly coated in the centre and red at the edges, sometimes moist, in other cases dry.

The subjective symptoms cannot be depended upon at all in the prodromal stage.

It is only in the premonitory stage or before the recognition of an epidemic of cholera that the disease is apt to be mistaken for any other. Typical cases are absolutely unique, and the diagnosis is easily established by the rice-water stools, the rapid emaciation, suppression of secretions, prostration, and algid condition. Nevertheless, errors have been made, and those diseases and conditions which have from time to time been mistaken for cholera, or for which cholera has been mistaken, are septicæmia, cholera morbus or cholera nostras, severe gastro-enteric fever, typhoid fever, pernicious malarial fever with gastro-intestinal symptoms, and ptomaïne or other forms of poisoning. Asphyxia from coal-gas (CO) poisoning may resemble the stage of choleraic asphyxia, but the absence of the rice-water stools will not long leave the diagnosis in doubt.

In the typhoid or septic condition into which cholera patients sometimes pass during the reaction stage the disease sometimes resembles typhoid fever, but the latter can be differentiated by the type of the fever, the abdominal eruption, the less rapid emaciation, and the fact that the stools, if diarrhœal, are much less watery than in cholera. In cases of severe septicæmia the invasion is less acute, the temperature is higher, there may be chills and sweating, and the history of the case is wholly different. Exceptionally, intensely acute cases of cholera morbus prove fatal in a day or two, and very closely resemble Asiatic cholera, although usually complete suppression of urine, cyanosis, and prolonged muscular cramps are wanting in the former disease. The bacterial diagnosis can be made within a few hours. The stools, while loose and watery, are not so clear as the typical rice-water evacuations of Asiatic cholera. The cases are almost always isolated, non-epidemic, and recovery is more frequent. In pernicious malarial fever of the gastro-enteric type the onset of the disease is often acute, and for a few hours it may resemble cholera, but the temperature is much higher, reaching 106° or 107°; free pigment is found in the blood, with sometimes malarial organisms.

Ptomaïne poisoning produces great prostration, violent watery diarrhœa, cramps, thirst, etc., but the history of the case and the non-appearance of typical rice-water stools will enable the diagnosis to be made. There are some cases of acute arsenical poisoning which may resemble the first stage of cholera from the collapse, cramps, suppression of urine, and thirst which may occur; but in these cases there is decided epigastric pain and burning, with constriction in the throat and œsophagus. In all doubtful cases thorough bacteriological examination should be at once made.

Prognosis.—The prognosis of cholera depends mainly upon the severity of a given epidemic and the promptness with which individual patients are treated. Other conditions which affect it are the general sanitary condition of environment and the patient's previous state of health. The prognosis is worse along the sea-coast than inland, and is always bad in overcrowded camps and tenements. In Asia, such are the habits of the people, so largely influenced by ignorance, superstition, and certain religious customs, that no progress has of late years been made in reducing the mortality from cholera, excepting where the British government has been able to improve the water supply and drainage in some localities, notably in Calcutta. By these means the mortality of foreign soldiers serving in India has been reduced to one sixth of the rate of thirty years ago, when it varied between 18 and 20 per 1000. In various epidemics the mortality has varied chiefly between 20 and 80 per cent., and it has sometimes been as high as 90 per cent. The mortality is greatest at the extremes of age when individuals are regarded, but in general the total mortality is greater in early adult or middle life, because more victims are taken during this period. Some extensive epidemics have had comparatively slight mortality, while others, less widespread, have been exceedingly fatal.

From 21 cases of cholera diagnosed by myself bacteriologically, and 1 clinically, only 4 deaths resulted: 3 died directly from the effects of the disease; the fourth, after becoming convalescent, contracted lobar pneumonia, to which he succumbed. Judging from these results, in which there is a mortality of less than 14 per cent., Asiatic cholera should not be considered such an excessively dangerous disease; in fact, it is an easy enemy to vanquish if one is well prepared for it and is forewarned of its presence.

PROPHYLAXIS.—Unquestionably, the greatest drawback to the total extirpation of cholera, which is theoretically quite possible if a sanitary millennium could be attained, is the ignorance, superstition, and fanaticism prevailing among different races and tribes of semi-civilized Eastern people. In the past few years many lives have been lost through riots originating in efforts on behalf of the people to prevent the enforcement of ordinary commonsense hygienic rules. Officers in authority in their attempts to use disinfectants, and even physicians making humane efforts to treat the disease, have been brutally mobbed. It will be long before this condition can be overcome, and such is the religious superstition prevailing in India in regard to bathing in the sacred pools and other religious rites, that it is doubtful whether the disease can ever be wholly controlled as it should be. It is possible, however, for civilized countries to protect themselves against invasion by the adoption and enforcement of simple sanitary regulations which have been thoroughly proven abundantly adequate to check absolutely the further spread of the disease.

Cleanliness.—In all epidemics of cholera a careful study of the modes of transmission of the disease emphasizes the fact that personal cleanliness and absolute cleanliness of all clothing are distinctly prophylactic. Upon guarded steamships, unless they have contracted the disease from foul water on shore, it never spreads among the well cared-for cabin passengers, but affects particularly emigrants of the low classes, whose filthy habits, combined with overcrowding, make them ready subjects to the infection.

Among other prophylactic agencies are the examination and disinfection of all emigrants coming from a region infected with cholera, their detention, by suitable quarantine regulations, on their arrival at a new port, their prompt treatment, isolation, and disinfection when suspicious cases occur, and finally the enlightenment of the general public as to the real nature of the disease and the impossibility of infection by any other means than through the agency of the mouth, because either contaminated food or drink is the agent necessary to originate an epidemic.

When an invasion of cholera is threatened, all cities liable to be invaded, especially seaboard towns, should be put in the best possible sanitary condition. The streets should be thoroughly cleaned; all sewers, cesspools, or receptacles for excreta or manure should undergo a most thorough cleansing and disinfecting. The water supply should be immediately investigated, and every source of contamination with it should be guarded, if necessary, by sanitary police. Through printed circulars and the public press the public should be warned to use no water for either cooking, drinking, or washing purposes (or brushing the teeth) which has not been first subjected to thorough and prolonged boiling, which will render it absolutely innocuous.

The local government should appoint special medical inspectors whose duty shall be to allay the fears of the people and disseminate knowledge in regard to the importance of obeying sanitary rules and caring for personal hygiene. They should make house-to-house visits and see that all cases of diarrhœa or dyspepsia from any cause are promptly treated. Large assemblies of people should be forbidden, especially at public funerals of those who have died from the disease.

Raw Food.—The eating of all forms of raw food should be discouraged, for undoubted cases of infection from this source are numerous. If necessary, the civic authorities of the town should take measures to prevent temporarily the sale of all fruits and such vegetables as are apt to be eaten raw. This was done in Hamburg during the last epidemic there. The reason for such action is obvious. The fruits and vegetables are often cleansed by washing them in foul water, and undoubtedly not only cholera, but typhoid fever germs, may be conveyed into the human body by eating raw food which has been thus contaminated. Moreover, it has been clearly proved that flies are active agents in spreading cholera bacilli abroad. Their filthy habits, in the exercise of which they alight on decomposing offal and excreta, cause the contamination of their feet and bodies with the germs of disease, which are thus easily conveyed by them to any articles of raw food, such as sweet, overripe fruits, etc., which are exposed on public sale. This is not mere theory, but the observation of scientific bacteriological research.

Much discussion has been occasioned in regard to the possibility of infection from beet sugar prepared in an affected locality, the idea being that the coarse sacks in which the sugar is shipped for commerce become saturated with saccharine material, affording a good culture medium for cholera germs; but Sternberg has proved that cholera bacilli do not grow in a moist beet sugar medium in the absence of nitrogenous material, and beet sugar alone does not nourish the spirillum.

Disinfection of Stools, Clothing, etc.—Physicians, nurses, and attendants are no more liable to contract cholera than they are in attending cases of typhoid fever to acquire that disease, and identical precautions must be observed. In both cases infection is conveyed through the stools, and absolute personal cleanliness after handling the patients or their evacuations cannot be too strictly insisted upon. In cholera the stools are so copious, and occur with such frequency and violence, that it is often difficult to keep the patients and their bedding clean, and the hands of the attendants must necessarily come more or less in contact with the evacuations. Unless they thoroughly disinfect themselves by washing the hands in soap and water, alcohol, and finally corrosive sublimate, a 1 : 500 solution, or 1 : 20 carbolic acid solution, they may convey the germs to their own food at their next meal, and thus become infected. Great care should be exercised by such attendants not to spatter any fluid into their own mouths while bathing cholera patients or washing utensils, bed-pans, etc. All clothing and bed-clothing of patients, if they cannot be burned, should be placed in disinfecting solutions before they are washed ; otherwise there is the same danger of infection for those who handle them by spattering the contaminated water about or immersing their hands in it. It is claimed that greatly debilitated patients who have been crowded in rooms or hospital wards with cholera patients, and who have been obliged to inhale effluvia from their evacuations, have contracted the disease, but under these conditions it is difficult to disprove the possibility of other sources of infection, such as those before described, and the poison must certainly be very concentrated to enter the system in any such manner.

All dejections must be received in china bed-pans containing either a 1 : 500 corrosive sublimate solution or a 5 : 100 carbolic acid solution. The volume of solution should be at least half of that of the stool to secure thorough disinfection, and it should remain in contact with it for an hour or two before being thrown away. Schauz and others advise the addition to the disinfectant of a solution prepared by adding 100 grammes of crude sulphuric acid to a litre of water. This is to be added to the stool in the proportion of one sixth of its volume. Other disinfectants are made more efficacious by the addition of this acid. The practical objection to this method is that the acid is ruinous to metallic drain-pipes, and to overcome this difficulty Stillé suggests that the dejecta after disinfection be either mixed with sawdust and burned or buried in a trench.

Quarantine.—When a vessel sails from a port in which cholera prevails or in which, during an epidemic elsewhere, suspicious cases of gastro-intestinal disorders have been reported, she should, on arrival, be held at quarantine until thorough bacteriological examination can be made, which is possible within twenty-four hours. If the result of the examination establishes the presence of cholera infection on board, all the passengers should be removed at once, and carefully separated into groups of the sick, the well, and suspected cases. Authorities differ as to the length of time which they should be detained, and many eminent sanitarians (especially in England) are disposed to ignore the necessity of quarantine for the well, believing that the disease can be readily stamped out in any situation in which it may occur. Others claim that all persons from the infected vessel should be held for from seven to ten days. In any event, their baggage should be disinfected by steam, and the vessel must undergo thorough disinfection by being flooded with steam and washed down with a 1 : 500 solution of bichloride of mercury. Emigrants who are suspected should be given an antiseptic bath, and their personal clothing and baggage should be disinfected in steam sterilizers under pressure. Since the disease is often spread by foul clothing, the importation of rags from infected ports should be absolutely prohibited during the prevalence of the disease.

The International Sanitary Conference, which met at Rome in 1885, adopted the view that a disinfection of the mails and of clean dry merchandise was wholly unnecessary.

During the prevalence of cholera epidemics on board ship it is impossible for the ship's surgeon to take the time or supply the facilities for bacteriological research, even were he competent to do the work of an expert. There is a strong tendency on the part of shipowners to conceal, for obvious reasons, the possibility of deaths from cholera occurring upon their vessels; hence it is that the doubtful cases are usually recorded as "gastro-enteritis." The fatal cases are promptly buried at sea, and all their effects are thrown overbroad. This greatly embarrasses the health officers in their work at quarantine, for it is often impossible upon the ship's entry into port to obtain a single article of personal clothing or of bedding which belonged to a fatal case, much less to obtain any of the excreta, for examination. It should be the duty of the ship's surgeon to preserve specimens of the dejecta in sealed receptacles for bacteriological examination, for it would thus be possible for the health officers to determine with greater certainty whether or not the ship has been infected with cholera. During the last epidemic of cholera in this country much time and anxiety might have been saved upon the ship's entering New York harbor had this precaution been taken.

TREATMENT.—There is as yet no specific treatment for cholera, although it is not impossible that an antitoxin or an immunizing serum may be before long discovered which will afford a means of checking this much-dreaded plague.[1]

The rational treatment of the disease is based upon the principles now established which govern the treatment of similar infectious diseases having a definite focus of operation for the activity of the pathogenic germs, from which poisonous materials or toxalbumins are developed to be absorbed by the agency of the lymphatic or blood-vessels, and thus cause general systemic intoxication. In the case of cholera the focus of the disease is a single one, very definitely located in the intestines. The appearance and nature of the germ is definitely known, as are also those remedies which are capable of destroying it. The problem of treatment is, then, a twofold one: first, to either destroy or limit the development and activity of the germs *in loco*, and, second, to combat the effects on the system of the highly poisonous substances which may have been already absorbed, and aid the process of elimination and reparation. Such is the extraordinary virulence of this disease that the former method offers more hope of successful accomplishment than the latter, although both methods are to be simultaneously employed. The treatment above outlined will be conveniently described under the headings of

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[1] The prophecy here made by Dr. Byron is possibly approaching verification since his untimely death. Dr. Haffkine, a former pupil of Pasteur, has for several years been experimenting with preventive inoculations against cholera. The inoculations are first made with a mild culture of cholera germs, and five days later with a stronger one. Five days later, still, immunity is reported to follow. Dr. Simpson, health officer of Calcutta, was authorized in the spring of 1894 to expend 20,000 rupees (approximately $5000) in research with the inoculations. His report to the Municipal Commissioners of that city, lately issued, covers a series of 7690 persons, chiefly Hindoos, who received the treatment. Of this number many were exposed to the disease before the lapse of five days after the second inoculation, but some of these escaped infection, or, being infected, escaped death. Of a smaller series of 269 persons inoculated five days or more before exposure, a few—Dr. Simpson does not give the exact number—became infected, but only 1 died. He claims that the chances of death among inoculated subjects are "22.62 times smaller" than they otherwise would be. Dr. Haffkine himself, experimenting in India, claims similarly favorable results. Judgment of the value of this treatment must be suspended until more extensive reports are received. As in the early days of the diphtheria antitoxine inoculations, much opposition is being made by some of the British physicians in India to the treatment, but it is to be hoped, as Dr. Byron has said, that success in this or a similar method may be attained when the technique of its application is fully understood.—EDITOR.

1. Internal antiseptic treatment;
2. Systematic treatment.

1. *Internal Antiseptic Treatment.*—Many remedies have, in times past, been strongly advocated for the purpose of limiting the local action of the cholera bacilli, and such remedies were, in fact, employed before the germ theory was established, but modern research and experience have reduced this number to a very restricted basis.

Calomel is strongly recommended by Von Ziemssen and others. It is distinctly serviceable in the premonitory stage and in mild cases as an evacuant of the poison from the intestine, and its probable partial conversion in the alimentary canal into a more strongly antiseptic form of mercury no doubt enables it to exert some slight disinfectant or germicidal action. I have, however, found it worse than useless in severe cases. Mercuric bichloride is used by Ivert and others. He employed it in Tonquin, and claims a reduction in mortality from 66 to 20 per cent. Iodoform has been recommended by Bouchard, and other remedies of the so-called intestinal antiseptic series which have been extensively tried are naphthol, naphthalin, salicylate of bismuth, salol, etc. All the above remedies possess the common disadvantage of being administered *per os*. There is usually persistent vomiting, which is intensified by all stomach medication. Moreover, most of these remedies are so altered in their transit to the real focus of the disease that they cannot be depended upon. Owing to their poisonous nature in large doses, it is unjustifiable to give them in strength sufficient to prove effective germicides against so active a bacillus as that of cholera.

2. *Systematic Treatment.*—The systematic treatment which follows is most strongly recommended from the results of my personal experience with cholera at quarantine. It will be conveniently divided to correspond with the natural stages of the disease.

(*a*) *Premonitory Stage.*—In the premonitory stage the patient should be kept in bed after receiving a warm bath, and must be carefully protected from cold. Ten grains of calomel may be administered, and intestinal irrigation should be at once begun after the manner described below (Enteroclysis, p. 329).

The food must be very simple, and it is best given in small doses at two-hour intervals. Such articles as boiled milk, thoroughly cooked rice, milk toast, and plain broths should be given. It is often best to pancreatinize the milk, and, as the gastric juice is feeble and intestinal digestion is disordered, it is well to give fifteen or twenty minims of dilute hydrochloric acid with five grains of pepsin after taking animal food. The acid destroys the cholera bacillus and prevents the development of its poison, besides being the natural acid of the gastric juice. It has the further effect of tending to slightly diminish the patient's thirst. These are the ordinary precautions to be taken in dealing with the premonitory stage, but every case of cholera, in whatever stage it may be first seen, should be subjected at once to intestinal irrigation.

The premonitory stage is often very brief, and is often unrecognized by either patient or physician, and in a majority of cases the physician is not called or does not reach the patient until the evacuant or collapse stage has developed. Those cases seen at Swinburne Island were of such an exceedingly virulent type that the premonitory diarrhœa was very slight and often passed unnoticed.

The administration of preparations of opium in the early stage of cholera to control the diarrhœa is to be condemned, for it may cause retention of the intestinal contents, and thereby counteract nature's only method of eliminating the poison of the disease by watery evacuations. Given later, it is usually ineffectual in controlling the discharges from the bowels, and it merely adds a dangerous narcotic to the system. Morphine may be required hypodermically, however, to relieve the cramps when in the later stages they become intolerable.

The treatment of the second stage, or stage of serous diarrhœa, does not differ essentially from that of the stage of collapse, and it will therefore be detailed under that heading.

(*b*) *Stage of Collapse.*—In this stage the most active and prompt treatment is an absolute necessity if the patient's life is to be saved. The main indication for treatment in this stage is to restore by every possible means the water which has been drawn from the blood in copious alvine evacuations.

During two epidemics I have obtained the most encouraging results from what I may call the surgical treatment of this stage—*i. e.* the injection of fluids into the body through the skin and rectum, as described below (Hypodermoclysis, Enteroclysis, p. 329). This method of treatment, resorted to at Swinburne Island, differs from all others, inasmuch as the internal administration of drugs is avoided. I first used this treatment in 1892, and, encouraged by the results obtained, I again used it in 1893 with still better effect, though it should be stated that the last epidemic was not of such a virulent character as that of 1892, and that most cases were treated at an earlier stage of the disease.

In former epidemics the attempt has been made to transfuse salt solution, defibrinated blood, etc. into the veins as a means of restoring the balance of circulation more promptly than in any other way, but the practical difficulties in the way of this procedure are considerable, owing to the fact that all the veins are collapsed, and are, consequently, difficult to find. It is often impossible to secure one large enough for transfusion without performing a formal operation to reach a deep-seated vein. Especially is this true in children, and the time lost in the procedure may be even greater than that required for the absorption of fluids administered in other ways, and the operation adds to the discomfort, if not the terror, of the patient. Practically, the method has proved an emphatic disappointment, and it is now rarely practised.

Hypodermoclysis.—This name is applied to the simple process of the free subcutaneous injection of a normal salt solution; that is, 0.6 per cent. of sodium chloride in distilled water, or, practically, two small teaspoonfuls of pure common salt to the quart of warm water, distilled and sterilized. It is often well to add an ounce of brandy, as stimulation is much needed. The operation of injecting this fluid was first suggested and used by Cantani of Naples in the cholera epidemic of 1865, and he has since then employed it repeatedly with great success. Its recommendations are its simplicity and the promptness with which it can be performed. To give the injections an ordinary rubber douche-bag is utilized, such as that commonly employed for vaginal irrigation. To the rubber tube leading from this bag a small-sized aspirating needle is attached. The bag is filled with the salt solution at a temperature of 110° F., which is reduced to 105° F. in its passage through the apparatus. A large fold of skin is grasped between the thumb and forefinger, and lifted so that the needle can be introduced deeply into the loose cellular tissue of the subcutaneous space. The skin, as well as the hands of the operator and needle, should all be first sterilized. The skin should be first washed with soap and water, and afterward cleansed with alcohol and ether and a 1 : 500 solution of bichloride of mercury. The needle should be boiled for at least half an hour. The point of selection for administering the injection should be preferably on either side of the abdominal wall between the inferior ribs and the iliac crest. In extreme cases the injection can be made into the peritoneal cavity. The inner surface of the thighs can also be utilized, but the region of the neck should be avoided, as two cases of laryngeal œdema are known to have occurred after the injections. When all these precautions are conscientiously observed no untoward results occur. I have known of but one accident—the development of an abscess—which was distinctly due to a careless observation of the above rules. The quantity of fluid injected for the first time by hypodermoclysis should be, for an adult, from one to two quarts; for an adolescent, one or two pints; and for an infant, one half pint. In critical cases the injection should be pushed as much as possible, and repeated again in an hour or two. The liquid enters by hydrostatic pressure, and the reservoir may be gradually raised or lowered to regulate it. About half an hour should be consumed in injecting a quart of fluid. The injections are not so painful as might be supposed. At all events, the patients are so ill that they submit to the treatment without much complaint, and, as the saving of time is an important object, the use of cocaine is not desirable, especially as it is decidedly depressant to the heart action in the doses which would be required to cover the ground of the injection. As an immediate result of the entrance of the fluid a large tumor forms which may reach the size of an orange, but it is not advisable to attempt to dispel it by massage. If the hypodermoclysis is successful, the tumor will soon be naturally absorbed, and in favorable cases its disappearance will be complete in from twenty to forty-five minutes. I regard the rate of absorption as of considerable prognostic value, for if absorption is delayed for three or four hours, it is an indication that the lymphatic and hæmic circulations are both very feeble and that death is likely to soon occur. More rapid absorption, on the other hand, with improvement in the volume of the pulse, is an exceedingly favorable sign. The introduction of the salt solution has a twofold beneficial action: First, by restoring the proper volume and normal density of the blood the circulation is benefited and the inhibited renal function is re-established; secondly, it acts favorably as a diluent of the ptomaïnes which have been absorbed from the intestines, and aids in their elimination from the system.

In favorable cases the effects of the injections are truly astonishing in their rapidity of action and in the change in the appearance of the patient. This method of treatment is indicated just as soon as there is the slightest appearance of the approaching stage of collapse, and it should be repeated according to symptoms until permanent restoration of the balance of the circulation and respiration has been established. Among those who commend this treatment as a result of personal trial are, notably, Cantani, Nothnägel, Kaeler, Rumpf, Von Ziemssen, and Stofella.

Enteroclysis.—To fulfil the second important indication for treatment it is necessary to reach the focus of the disease by intestinal irrigation. There is the more hope of benefit from this procedure from the fact that comma bacilli affect the superficial layers of the intestinal mucous membrane, and are, consequently, within reach. The difficulty or impossibility of oral medication has been already discussed, and it remains to be proven that fluids introduced in large volume *per rectum* can be made to flood the whole intestine. This fact is often denied, for it is claimed that the anatomical structure of the ileo-cæcal valve completely prevents regurgitation from the large into the small intestine. That this is ordinarily true under normal conditions there can be no doubt, but it is, nevertheless, also true that under moderate hydrostatic pressure fluids may be made to pass this valve. The conditions for its successful passage are the use of a long and properly introduced rectal tube, a large volume of fluid, a hydrostatic pressure of about five feet, a horizontal or partially inverted position of the patient, and the performance of gentle massage, commencing in the right iliac region and passing in the direction of the ascending colon. To test the possibility of the passage of the fluid beyond the ileo-cæcal valve I have made experiments on a number of cadavers, and have been able to fill not only the entire intestine, but even the stomach, in the manner described. These results are confirmed by Cantani, Simon, Hofmolk, and Hegar, and they are further confirmed by the fact that in several instances where I have used tannic acid injections for cholera patients some of the acid has been ejected by vomiting. In some experiments upon cadavers I have even succeeded in forcing the passage of liquids from the rectum out through the mouth and nose by means of no harder pressure than that which is justifiable in the clinical treatment of cholera. There are undoubtedly some cases in which, owing to a twist in the large intestine, old adhesions, disproportion in the size of the valve, or other conditions, it may be impossible to reach the small intestine, but even in these cases the large intestine can almost always be completely flooded. The rapid emaciation of the patient and the consequent thinness of the boat-shaped abdominal walls makes it comparatively easy to manipulate the intestine by massage.

Method of Giving the Injections.—The ordinary fountain rubber douche-bag is employed, or, in an emergency, a quart bottle may be fitted with a piece of rubber tubing, and when the bottom is knocked off it may be suspended inverted and used as a reservoir. The rubber tubing is connected with a long rectal tube which should have a blunt extremity and one or two large perforations situated from one to two inches behind the blind end. Such tubes as those employed for stomach washing are of suitable size and stiffness. If too stiff, they do not readily follow the curves of the rectum, and if too limp, they bend or twist, which makes their introduction difficult. Such a tube can always be passed in for a distance of seven or eight inches, and occasionally, with good luck, it can be made to pass beyond the sigmoid flexure. All the apparatus employed is to be sterilized, and the water used for the injection should be distilled and sterilized. The tube is well oiled and carefully passed into the rectum. Sometimes its further passage can be facilitated by allowing some of the fluid to flow while the tube is pressed inward.

The object of the injections is a threefold one: First, to flush the intestine and wash out such poisonous material as may be within reach; secondly, to supply a medium fatal to the comma bacillus; thirdly, the fluid being hot, local warmth is applied to the deeper portions of the body, which is serviceable in arousing the patient from collapse. These indications are met by the use of a 2 per cent. solution of tannic acid in water, heated in the reservoir to 110° F. A lowering of about five degrees in this temperature occurs as the fluid flows through the rubber tubing. It is well to warm the rectal tube in hot water before its insertion. When the tube is in place the injection should be allowed to flow at first very slowly, and fully ten or fifteen minutes should be occupied in giving a quart or more of fluid. After the fluid has been injected, several minutes more should elapse before the withdrawal of the tube, while gentle pressure is maintained on the perineum, and the patient is to be encouraged to make every effort to retain the injection. The tube is then very slowly and carefully withdrawn. By means of these precautions it may be possible to secure the retention of the injection for some time. This will check the growth of the bacillus, and much of the fluid may be absorbed by the lymphatics. The quantity of fluid to be employed should be from one to two quarts, and in severe cases it is to be used as often as once every hour.

Other remedies which have been used by rectal injection are solutions of subacetate of lead, solutions of creolin (2 per cent.), and diluted laudanum.

With regard to the efficacy of the treatment by hypodermoclysis and enteroclysis the following data are instructive, but it should be borne in mind that the patients treated at Swinburne Island were many of them brought off the vessel in an almost moribund state. There were in all 72 cases treated in the epidemic of 1892 at Swinburne Island, with 20 deaths, giving a mortality of 27 per cent.; or, if 46 suspects are included who had distinct prodromic symptoms of cholera, the mortality is reduced to 17 per cent. On the other hand, among the patients attacked at sea upon the vessels which reached our quarantine the mortality varied from 50 to 98 per cent., and the general mortality of this epidemic in Hamburg was between 50 and 60 per cent. Undoubtedly, the mortality at Swinburne Island would have been even lower but for the fact that many of the patients attacked were under-fed Russian emigrants, already anæmic or diseased. Many of them were marasmic young children, so that the premonitory stage of the disease was often absent.

Application of Warmth.—In the stage of collapse the external surface of the body is always cold, and the external temperature may be six or eight degrees below the normal. To restore the natural warmth and aid in the re-establishment of the normal circulatory functions external heat must be energetically applied. In many cases this is best accomplished by the use of a hot plunge bath, which has the further advantage of diminishing the tendency to cramps. While in bed the patient should be kept warm by the use of hot water bags, hot sand bags, or hot bricks packed about the extremities, or hot air may be applied beneath the bedclothes. The latter should consist of two woollen blankets and a counterpane. As before indicated, heat is also supplied in some degree by the warm subcutaneous and rectal injections given. If perspiration occurs, the sweat should be immediately dried.

Relief of Pain and Cramp.—When the cramps are unbearable they should be relieved by inhalation of chloroform to the point of primary anæsthesia. Moderate cramps are sometimes relieved by the rubbing of the muscles with mustard water, by the application to the abdomen and legs of hot water bottles or of turpentine stupes. Placing the patient in a bath of 108° F. for twenty minutes will sometimes give great relief. Care is of course to be exercised in moving the patient, and he should be lifted so as to be subjected to as little exertion as possible.

When the patient's general condition is one of great suffering, small hypodermic injections of morphine (one sixth of a grain), combined with one one-hundreth of a grain of atropine, should be given locally in the muscles chiefly affected. It is noticeable that in cases of cholera treated by subcutaneous and rectal injections the frequency of pains and muscular cramps is greatly diminished. This is a further proof of the belief that the cramps are directly due to the drying of the muscles and nerves which follows the loss of water from the intestines.

Relief of Vomiting.—When the vomiting is excessive it may be sometimes relieved by hypodermic injections of morphine, and by a mustard paste or turpentine stupes applied over the region of the stomach. The aërated waters, small doses of iced champagne, or iced fresh lime juice are sometimes grateful for relieving thirst and to some extent controlling the vomiting; but, as a rule, throughout the entire stage of collapse, if there is any nausea or tendency to vomiting, it is best to make no attempt to give anything at all by the mouth. The mechanism of vomiting only excites further intestinal movements in a reflex manner, and is weakening and injurious. When vomiting is persistent and the ejecta are copious, it is desirable to wash out the stomach by lavage. For this purpose a hot 2 per cent. tannic acid solution is to be employed, like that recommended for enteroclysis. The removal of the cholera liquid from the stomach will check further vomiting and straining, and will add much to the patient's comfort.

Stimulation.—While the stomach remains irritable stimulation is to be given in connection with the hypodermoclysis or by separate hypodermic injections of brandy. The ordinary hypodermic syringe, holding half a drachm, may be filled with good brandy, which is to be deeply injected in the outer side of the arms or thighs. Several such injections should be given, at least once an hour. For an infant five or ten minims may be used.

The entire stage of collapse is to be combated by vigorous hypodermic stimulation, for which purpose such remedies are to be used, in addition to brandy, as sulphuric ether, strychnine, gr. one thirtieth, citrated caffeine, gr. j, and morphine, gr. one sixth. Efforts to stimulate by the mouth do more harm than good. In this stage, especially when dyspnœa is prominent, the free inhalation of oxygen gas is often beneficial, or at least it relieves the subjective sensations of the patient. Nitrite of amyl inhalation is also of occasional benefit.

(*c*) *Stage of Reaction.*—Should the suppression of the urine continue into this stage, the rectal and subcutaneous injections should be continued two or three times a day, but it is undesirable to use tannic acid. If the temperature becomes normal, the external application of heat is discontinued, and should a reactionary fever occur the patient's woollen undergarments and heavy bedclothes should be removed.

As the symptoms begin to abate and slight improvement is manifested, a little fluid nourishment may be cautiously given *per os.* Aërated waters may be freely given. For this purpose may be used one of the meat extracts, pancreatinized milk, or koumyss. The milk is often better borne if diluted with equal parts of Vichy or carbonic water. Iced champagne in tablespoonful doses is also to be recommended.

Throughout convalescence the patient must be carefully watched, and the return to solid food must be very gradually made, attention being given to the condition of the bowels and gastric digestion. The stomach often remains very weak for many days, and the patient must be kept upon a diet of predigested milk, beef peptonoids, nutritious broths, and gruels, egg albumen with sherry, milk punch, or egg-nog.

Later, such articles may be given as cream toast, junket, well boiled rice, lightly cooked eggs, custards, meat broths thickened with rice or macaroni, etc.

As soon as more food is given, it is best to resume the administration of dilute hydrochloric acid and pepsin, which may be given every three or four hours.

Strychnine may be given as a tonic, at first hypodermically two or three times a day, and then by the stomach in doses of one fiftieth of a grain. Later the simple bitters and preparations of malt may be useful, and three grains of quinine may be given as a tonic after each meal.

The urine should be frequently examined until all albuminuria has disappeared. If the kidneys are slow in resuming their normal activity, mild saline diuretics and effervescing mineral waters are to be prescribed.

The patients at Swinburne Island were compelled to take a daily sun bath, which proved of great benefit.

I quote in full the details of three cases from my contribution to the *Report of Health Officer, Port of New York*, 1893, which are selected from the clinical notes of Dr. Judson Daland, who volunteered as assistant during the late epidemic at Swinburne Island. They will be found to present an instructive clinical picture of the symptoms and a résumé of the treatment employed :

CASE I.—" Male, twenty-nine years ; passenger on board S. S. Karamania ; in perfect health until the 3d of August, 1893, when he began to have a moderate diarrhœa and nausea. Not considering his illness serious, he did not report his condition until the afternoon of the 6th, when his symptoms became alarming. When examined by me the same day I found him in collapse, with the following symptoms : Pulse rapid, filiform, and compressible ; temperature subnormal, features pinched, eyes sunken, injected, and expressionless ; lips, eyelids, and extremities cyanosed ; cold, clammy perspiration ; husky voice ; complete indifference to all surroundings ; intelligence unimpaired. Patient complains of excessive thirst and a choking sensation, which he describes as if having a heavy weight upon the chest. Vomiting and rice-water discharges abundant and repeated at short intervals.

" Examination of dejecta showed comma forms mixed with other bacteria ; cultures on bouillon and gelatin revealed the bacilli of Asiatic cholera. Patient was transferred to the hospital and subjected to the following treatment : Hourly rectal injections of the hot 2 per cent. tannic acid solution ; subcutaneous injections of brandy, preceded by a single injection of $\frac{1}{100}$ grain of nitroglycerin. The condition of the patient grew rapidly worse. At midnight his temperature (rectal) was 96° F. ; pulse only perceptible at the brachial artery ; profound collapse. Three quarts of sterilized salt solution (salt 1 part, water 1000) were injected into the peritoneal cavity after proper disinfection of the skin and instruments. Rectal injections were also continued. From this time symptoms began to improve. Six hours later all the fluid had been absorbed from the peritoneal cavity, the radial pulse could be perceived, the respiration was easier. A second intraperitoneal injection of two quarts of warm salt solution was injected, and the rest of the treatment continued.

" August 7.—Improvement continued. As vomiting had ceased, the patient was allowed to take some beef tea and milk and seltzer. Rectal injections continued ; hypodermic stimulation suspended. Diet carefully increased until the morning of August 10th, when all treatment was suspended and the patient was taken out for a sun bath. Recovery. Duration of disease from first symptoms to convalescence, six days."

CASE II.—" The second case well illustrates an ordinary attack of Asiatic cholera. A Russian, aged seven years, was admitted from the steamship Bohemia, September 26, 1892, at 8 P. M., with a temperature of 96.2° F., pulse 106, respirations 22, and the surface of the body extremely cold and cyanotic. The face was pinched, especially in the nasal region ; it was markedly cyanotic, and the eyes were deeply sunken and surrounded by dark circles. The pulse was feeble and small, and was counted with difficulty. She at once received a warm plunge bath, and her stomach was then washed out with one pint of a 1 per cent. solution of tannic acid at the temperature of the body. Shortly afterward she vomited twenty-three ounces of fluid. She remained in about the same condition during the night, but the passage of a moderate amount of urine encouraged us to hope for a favorable issue. On September 27th her pulse was 104, temperature 97.4° F., and respirations 18. The cyanosis persisted; there was no further vomiting, but she had frequent copious discharges from the bowels, composed chiefly of the tannic acid solution which had been injected *per anum*. Later in the day improvement began; the temperature varied between 100.2° and 100.4° F.; a large semi-solid stool was passed. She slept moderately well during the night, but complained greatly of thirst. A sufficient quantity of urine was excreted, and the liquid from the bowels was composed chiefly of the tannic acid solution that had been given by injection. She became very restless, but the following day was much brighter and began to notice her surroundings. The dejecta changed in character, becoming greenish in color and somewhat frothy. On September 29th she slept well; her bowels were moved only after giving the intestinal injection of tannic acid solution. In the afternoon her improvement was so marked that it was decided to suspend these injections. Her temperature varied from 97.8° to 99.4° F., the pulse between 96 and 120, and the respiration from 22 to 24. On September 30th she was able to take nourishment and stimulants by the mouth, but the stools continued brownish and thin, and when an attempt was made to administer beef tea or any food by the mouth vomiting occurred. The cyanosis disappeared, but she was still shrunken and emaciated. She continued to improve, and on the fourth day after admission was carried into the open air, where she received a sun bath for two hours.

"The following is a summary of the treatment: Upon admission she received a hot plunge bath. The first enteroclysis or intestinal injection was retained for three minutes, and afterward these injections were repeated every two hours. A subcutaneous injection of one pint of a 0.6 per cent. solution of sodium chloride was given the day after admission. At first whiskey was administered by the mouth, but afterward 10 minims were given hypodermically every four hours. The total duration of the patient's illness was five days, and her convalescence was extremely rapid and uninterrupted."

CASE III.—"I will narrate the history of a third case, the most interesting of all observed, in which we were fortunately able to note minutely every change that took place from the beginning to the end. This patient exhibited nearly all the symptoms of a typical malignant case of Asiatic cholera, illustrating also, in an equally striking manner, the results obtained by treatment.

"This patient, a male, aged twenty-four years, a native of Germany, was admitted to the Swinburne Island Hospital on September 27, 1892, at 11 A. M. His muscular and osseous systems were unusually well developed, and it was reported that he was perfectly well on the morning of September 27th until 4 A. M., when he first complained of pain in the abdomen, which was followed by two loose stools. He continued feeling well until we saw him at 10 A. M., when, in view of the diarrhœa, it was deemed wisest to remove him to the hospital, although his general condition did not indicate that he was suffering from cholera. He objected strongly to his removal, and said that he felt perfectly well. He walked from his berth to the side of the ship and down a rope ladder to the quarantine tug-boat. He arrived at Swinburne Island, and reiterated his statement that he felt perfectly well, and walked from the quarantine boat to the door of the hospital, when suddenly he complained of weakness in the knees and fell to the ground in a state of collapse. He was carried to the ward in a condition of partial stupor, from which he was easily aroused. He responded to all questions in a manner showing that his consciousness was perfectly preserved. Soon he complained of agonizing cramp-like pains in the arms, feet, and knees, which recurred more or less regularly at intervals of thirty minutes. Immediately after his admission his countenance presented the typical appearance of cholera. The eyes were deeply sunken and surrounded by dark circles; the pupils were contracted to the size of a pin point. The lips, cheeks, arms, hands, legs, and feet were cyanotic, and the entire skin surface was dry, and when the skin was pinched it remained elevated and compressed for several minutes. There was no pulse at the wrist. The temperature was 98.5° F., the respirations shallow and 18 per minute, and the voice whispering. I was unable to detect any special coldness in the expired breath.

"The man was at once placed in a hot plunge bath having a temperature of 104° F., and was given four pints of a 1 per cent. solution of tannic acid at a temperature of 104° F.; also two pints of distilled water at a temperature of 100° F., containing 0.6 per cent. of sodium chloride and 1 per cent. of whiskey. He responded but slightly to this treatment; the pulse was scarcely perceptible, was filiform in character, and about 100 per minute. At 11.30, or thirty minutes after his admission, he complained of intense agonizing pains in the legs, feet, and hands. These cramps forced the feet into extreme extension and twisted and distorted the fingers. The pain was so great that it became necessary to administer a hypodermic injection of $\frac{1}{8}$ grain of morphine. The hypodermoclysis and enteroclysis were repeated. Camphor was given hypodermically. Oxygen was inhaled constantly, hot bottles were applied to the extremities, and hot air was conducted under the bedclothing from a large steam radiator. The patient now vomited a large quantity of a clear liquid, and passed several copious rice-water discharges from the bowels. His collapse deepened; the pulse became slow, feeble, and almost imperceptible, and his respirations shallow. His intellect was clear, and his condition is best described by the word 'terror.' At 2.30 P. M., or three hours and thirty minutes after admission, he was extremely restless and anxious, and the choleraic intestinal discharges continued. He moved from side to side, tossing the arms about wildly and calling aloud for air. The hypodermoclysis was repeated, and hydrochloric acid and brandy were administered by the mouth. At 5 P. M. he was pulseless, and complained most bitterly of intense pain, produced by the tonic spasm of the muscles. The cramps were so violent that the muscles were knotted and felt board-like. At 6 P. M. the hypodermoclysis was repeated; the pulse was scarcely to be felt, and thirty minims of whiskey were given hypodermically and repeated for five doses, but with no effect. He now passed two copious liquid stools containing whitish shreds composed of intestinal epithelium, giving the discharges their rice-water like appearance. At 6.30

P. M. he passed three more stools, and at this time we were unanimously of the belief that he must speedily die. At 7 P. M. he showed slight reaction; his extremities became a trifle warmer and the pulse more easily counted. At 10 P. M. hypodermoclysis and enteroclysis were repeated, and a hypodermic injection of twenty minims of whiskey was given every thirty minutes until 1 P. M. At 11 P. M. the intellect was clear; the eyes were horribly sunken and surrounded by dark circles; the nose pinched; the face shrunken; the voice whispering, and so feeble that the man was compelled to rest between words in replying to questions. He now complained of pain in the chest and renal region. His extremities grew warmer, and perspiration was visible on the trunk. This symptom was peculiar and rare, as in none of our other cases was perspiration visible in this stage. The mental condition—terror—persisted. At this time he ejected large quantities of rice-water liquid by five acts of emesis. A 1 P. M., September 28th, the slight improvement continued, and the hypodermoclysis and enteroclysis and hypodermic injections of whiskey were repeated. At this time he had three movements of the bowels, which were composed of the tannic acid solution given by injection. At 5 A. M. hypodermoclysis and subcutaneous injections of whiskey were repeated, the improvement became quite marked, and he slept quietly for a few hours. At 8.30 A. M. the enteroclysis was repeated and the whiskey was suspended.

"At 9 A. M. his physiognomy underwent a truly remarkable change for the better; the face became slightly flushed, the ghastly, death-like pallor disappeared, the expression about the eyes became more natural, and the entire skin surface, especially that of the extremities, was warm, and the pulse was of full volume, soft in quality, regular, beating 100 per minute. At 11 A. M. it seemed incredible that such wonderful changes could have occurred in the twenty-four hours which had just elapsed. At 10.30 A. M. the enteroclysis was repeated, and at 10.50 A. M. the pulse was full, regular, soft, and 88 per minute; the respirations were normal, and the expression good. He responded intelligently to questions and improvement continued.

"In both flanks, where the needle had been inserted repeatedly for the subcutaneous injection of the sodium chloride solution, the tissues were hyperæmic and sensitive to the slightest touch. No extravasation of blood occurred, and in three days these symptoms disappeared. At no time was a single drop of urine excreted. In ordinary cases the rate of absorption, after the hypodermoclysis, varies between forty and sixty minutes, whereas in this case three hours were required, thus showing that the power of absorption had been almost abolished. So soon as the liquid was absorbed a second enteroclysis was given. Hypodermic injections of twenty minims of whiskey were repeated almost hourly until midnight. The man passed a good night, vomiting but twice, and had dark-colored stools. His general condition remained unchanged. On September 29th he received champagne, and now recognized that he was convalescent. He was given whiskey and seltzer water, equal parts, every three hours, and at 10.45 A. M., for the first time, precisely forty-eight hours after admission, he passed one pint of urine. The examination of this urine showed a distinct trace of albumin; no sugar; specific gravity 1024; acid reaction, and the sediment contained numerous granular tube-casts. The liquid movements continued every two hours, and again he passed a normal quantity of urine. On September 30th the diarrhœa continued to average one stool every two hours; the quantity passed was small and the color had become dark. The patient was excessively irritable and nervous. He improved slowly for two days, and then sank into a typhoid state. There was no enlargement of the spleen or elevation of the temperature.

"As was feared, but little improvement occurred, and the typhoid state continued until death, which took place on October 5th, or eight days after admission to the hospital.

"The post-mortem examination revealed the ordinary changes that are found in cholera; the kidneys showed a severe grade of acute parenchymatous nephritis."

DYSENTERY.

BY HAMILTON A. WEST, M. D.

DEFINITION.—Under the term dysentery is embraced a group of morbid conditions affecting chiefly the large intestine, characterized by similar symptoms, but differing essentially in etiology, clinical course, and pathological results.

In attempting to give a definition of dysentery which would include the various forms, one meets with the same difficulty he would encounter in the effort to define under one category the different types of pneumonia.

Woodward, in his exhaustive study of diarrhœa and dysentery, despairing of improving upon any of the old definitions, does not offer a new one, but, following Trousseau, "embraces under the designation acute dysentery all the various forms of acute alvine flux, whether mild or severe, in which tenesmus is a prominent symptom." While this event is important as indicative of an inflammation of the colon and rectum of sufficient intensity to make expulsive efforts painful, and may serve, in many instances, to differentiate diarrhœa and dysentery, it is important not to misinterpret its diagnostic significance. There is abundant evidence to show that tormina and tenesmus may be entirely absent in cases which are proven to be dysentery by the autopsy, and, on the other hand, that various local causes, as piles, ascarides, intussusception, ulcers of the rectum, fissures, vesical calculi, tumors, and inflammatory conditions in and around the uterus, may be productive of tenesmus in the absence of dysentery. The presence of any symptom, however important, is insufficient to characterize the disease.

The following will serve as an illustration of the prevalent conception of dysentery as given by recent writers:

"By dysentery is meant a disease of the colon which appears sporadically, but more often in epidemics; it is excited by infection with an organized pathogenic poison about which we have as yet no further knowledge" (Strümpell).

The fundamental error in such definitions has been well pointed out by Ball, in that dysentery is regarded "as a morbid entity, an infectious disease expressing itself by an inflammation of the large intestine, essentially the same in its sporadic, endemic, and epidemic forms, in tropical climates and northern latitudes, and varying in its symptomatology and pathology in different cases only in accordance with climatic and other modifying conditions."

It comports better with our present knowledge to broaden the term for a group of inflammations of the colon chiefly, which may be of specific infectious or non-specific origin, which, differing however widely in causation, pathology, and results, are nevertheless characterized by a similarity in symptoms.

The following classification is here adopted in conformity with recent usage, and, though objectionable from the fact that it is based both upon the nature of the lesions and the causes, it is practical, for the reason that the forms described can usually be differentiated during life: viz. (1) acute catarrhal sporadic or non-specific dysentery, including those cases where the rectum is chiefly involved; (2) diphtheritic dysentery; (3) amœbic or tropical dysentery; and (4) secondary dysentery.

ETIOLOGY.—This constitutes one of the most important divisions in the study of dysentery, for from a knowledge of the causes only can there be developed an intelligent and successful system of prophylaxis. It is difficult to realize in northern latitudes, where this disease prevails usually in mild and sporadic forms, that it takes rank in malignancy and mortality with yellow fever, smallpox, and cholera as one of the four great epidemic diseases of the world. It is the scourge of armies, causing more sickness and death than any other disease, patients with dysentery and diarrhœa rivalling the wounded in multitude, and constituting a large proportion of those discharged for disability.

Climate.—While dysentery may occur in temperate regions in epidemic form at times, it is notoriously prevalent in tropical and semi-tropical regions, as in the East and West Indies, China, Africa, South America, Mexico, and southern portions of the United States of America.

Season.—In these regions the effect of heat as a predisposing factor is shown by the increased number of cases occurring during the hot months. It has been supposed that heat acts by producing an injurious operation upon the alimentary canal, leading to increased excitability and disordered secretion, but it is more probable that its effects are produced by aiding in the development of the special pathogenic organism, as it does in paludal fever, and explaining the fact, as mentioned by Aitken, that in every country where that disease exists dysentery is an endemic and prevailing disease.

Age.—No age is exempt from dysentery. Adults are more liable to the diphtheritic and amœbic forms than children, simply because of greater exposure to the exciting causes; but if we regard inflammatory diarrhœa or entero-colitis as synonymous with dysentery, then it is a disease of great frequency and mortality in children. Unquestionably when this disorder in children has lasted any considerable length of time, we find similar lesions to those found in the dysentery of adults, even in the absence of the ordinary dysenteric symptoms.

Sex.—The male sex is more liable to contract this disease than the female, simply from greater exposure to the exciting causes. Thus, out of 15 cases of the amœbic form reported by Councilman and Lafleur, only 1 was a woman; of the 7 cases reported by the writer, all were men. When we consider the extent from which men suffer the evils incident to the insanitary conditions of camp, army, and prison life, which have so much to do with dysentery, we can appreciate the preponderance of its prevalence in this sex.

Geological Conditions.—Various circumstances concerning the soil may predispose to dysentery by favoring contamination of drinking water, but as reference will be made to this subject farther on, it is unnecessary to enlarge upon it here.

Meteorological Influences.—Changes in the weather and temperature undoubtedly act as predisponents with regard to dysentery. Thus, it has been observed that sudden reduction of the temperature in the night, as is of common occurrence in the autumn season, or exposure to rain or heavy dews, will be followed by an increase in the number of dysentery cases.

Unhygienic influences, such as have heretofore prevailed in armies, fleets, and prisons. Dysentery has followed the track of all the great armies which have traversed Europe during the continental wars of the past two hundred years. It helped to destroy the British army in Holland in 1748. It decimated the French, Prussian, and Austrian armies in 1792. It was the chief cause of death in the ill-fated Walcheren expedition in 1809. It cut down the garrison of Mantua in 1811–12. It was the most fatal disease in the Peninsula campaign, and disastrous to the British troops in the Crimea in 1854. It is the disease of famished garrisons in besieged towns, of barren encampments, of starving prisoners, and of fleets navigating tropical seas.

Dysentery and diarrhœa were of enormous frequency in the Federal and Confederate armies during the Civil War in America from 1861–65. As stated by Woodward: "These disorders occurred with more frequency and produced more sickness and mortality than any other form of disease. They made their appearance in the very beginning of the war, not infrequently prevailing in new regiments before their organization was complete, and although, as a rule, comparatively mild at first, were not long in acquiring a formidable character. Soon no army could move without leaving behind it a host of victims. They crowded the ambulance trains, the railroad cars, the steamboats. In the general hospitals they were often more numerous than the sick from all other diseases. They abounded in the convalescent camps, and formed a large proportion of those discharged from the service for disability. Many of the prisoners upon both sides suffered and died from dysentery. For many months after the war was over and most of the troops had returned to their homes deaths from chronic diarrhœa and dysentery contracted in the service continued to be of frequent occurrence among them." What explanation can be given of this excessive morbidity and mortality from intestinal fluxes in army life? The reply must be that it lies in the infraction of almost every item of sanitary law which is incidental to, and so far has appeared to be inevitable in, times of war.

The lowering of vital resistance from overcrowding, irregular habits, exposure to bad weather, forced marches, want of rest, intemperate eating and drinking, bad cooking, and imperfect quality of the food, by producing intestinal catarrh provide a suitable soil for the growth and development of pathogenic organisms, which in the opinion of the writer are most apt to gain an entrance through contaminated drinking water, such polluted water supply being specially apt to occur in camps and armies.

Before discussing the methods of water infection mention should be made of other causes which are mainly predisposing.

Errors of diet have been regarded from time immemorial as potent factors in the production of dysentery. Articles which have been considered as most obnoxious are unripe fruit, decomposing vegetables, tainted meat, canned fish, meat, and vegetables. Such articles are more liable to cause diarrhœa, nature thus getting rid of the irritant substances. Occasionally, however, such dietetic errors result in a catarrhal proctitis, which rapidly subsides when the offending cause is removed. Dysentery is not likely to result unless the error is frequently repeated, but the catarrhal condition ensuing upon dietary faults will undoubtedly predispose to the worst forms of the disease. The idea that fresh fruits and vegetables are dangerous has been proven to be a mistake; on the contrary, army experience has demonstrated that by warding off scurvy and maintaining a better state of general health dysentery is actually prevented when such articles are freely consumed.

Constipation, and Retention in the Bowels of Fermentative Irritant Compounds.—Virchow and others have attached great importance to such conditions as causes of dysentery. Several circumstances show that this view is true of a certain class of cases, or at least that such influences predispose to dysentery—viz. the catarrhal and diphtheritic inflammation, ulceration, sloughing, and perforation of the mucous membrane in contact with fecal masses which accumulate above the point of obstruction in cases of stricture, and the fact that constipation often precedes the occurrence of dysentery, are significant in this direction.

Constitutional Condition of those Exposed.—Various writers on diseases of camps and armies have called attention to the effects of exhaustion from fatigue, over-exertion, loss of sleep during long marches, sieges, battles of several days' duration, as predisposing to dysentery.

In a like manner, any severe constitutional disorder producing general debility favors the development of dysentery among those exposed to its exciting causes. Thus, Finger, in describing the Prague epidemic, calls attention to the frequency with which the disease attacks patients already the victims of tuberculosis, cancer, typhus fever, syphilis, and Bright's disease. Woodward confirms these observations, and adds that in the American Civil War the diseases in which dysentery occurred principally as a secondary affection were tuberculosis, typhoid fever, malarial fever, and scurvy, and that in tuberculosis and typhoid fever there was not only the intestinal ulceration peculiar to these diseases, but in many instances acute catarrhal and diphtheritic dysentery developed as the terminal event.

As regards malaria and the scorbutic taint, the evidence is conclusive that the cachectic condition produced by these diseases is especially favorable for the development of dysentery.

Drinking Water.—In regard to contamination of drinking water as a source of infection, it has been conclusively proven that the infectious micro-organisms of cholera and typhoid fever (intestinal diseases) also are largely conveyed by means of impure water. It will be shown that there is at least a strong probability for such an origin in many cases of dysentery. When we consider the large quantity of water consumed by every individual, the extreme likelihood of its contamination with pathogenic organisms, and that, unlike the food, it usually is taken without any previous preparation by which such infectious agents might be destroyed, we can appreciate the influence a poisoned water supply might have as an excitant of this disease.

From the earliest times the use of impure drinking water has been considered as a cause of intestinal fluxes. Hippocrates discussed the question at length, and attributed the occurrence of such disorders among those who live in marshy districts to drinking the stagnant water of lakes and ponds. This opinion was quoted by Galen, who pointed out the methods of purifying water by filtration and boiling.

It is unnecessary to discuss at length the various ingredients of water which have been supposed to exercise a causative influence in the production of dysentery. Evil effects have been ascribed to inorganic substances in suspension and such substances in solution as sulphate and carbonate of lime, salts of soda, potash, and magnesia. The evidence upon this subject appears to be that, while such waters may often have a purgative effect, especially upon those unaccustomed to their use, and may be deleterious in other ways, there is no proof to show that these chemical ingredients will cause dysentery. Facts appearing to offer such demonstration—*e. g.* where in an epidemic of dysentery only those who drank limestone water were affected, those who used cistern water being entirely exempt—do not prove that the carbonate of lime was the morbific agent, but only that such water, being supplied by surface drainage, was liable to other contamination.

The presence of decomposing matters of vegetable origin in the water used for drink has been regarded as a cause of intestinal flux, but so far the evidence from either custom or experiment has been inconclusive as to the evil effects of such substances.

Pathogenic Micro-organisms in Drinking Water.—Since the facts as regards this source of infection have been established as to typhoid fever and cholera, the probability of a similar origin of dysentery has been greatly strengthened, and in the opinion of the writer ample confirmation will be offered when similar methods of investigation have been applied to dysentery; and here, also, fecal contamination is the most probable source of infection. I will cite but a few of the facts which go to support this view.

Read relates that in August and September, 1870, one of two regiments lodged in the barracks at Metz suffered greatly from dysentery, while the other had but few cases. On inquiry it was found that the former obtained its drinking water from two wells which were proved to have been contaminated with fecal matter filtered from neighboring latrines, while the latter drank from two wells not having such connection. The impure wells were closed and the disease at once subsided.

Oaks traced an outbreak of dysentery at Cape Coast Castle, on the west coast of Africa, to the passage of sewage from a cesspool into one of the tanks supplying drinking water.

One of the most conclusive instances upon record of water infection is that mentioned by Fagge in regard to the prevalence of dysentery in the Millbank prison. It appears that this disease had prevailed extensively and for a long time in this prison. Fagge says: "In the year 1854 the prisoners ceased to be liable to dysentery, and during the next eighteen years (up to 1872) one death only occurred from that disease or from diarrhœa; indeed, so far as I am aware, the immunity has continued down to the present time. Now one, and only one, change in its hygienic arrangement has coincided in time with this improvement in the sanitary state of the prison. Formerly the water which the convicts drank was taken directly from the Thames as it ebbed and flowed beneath the walls. But on August 10, 1854, the artesian well in Trafalgar Square was made the source of supply to the prison; this has since continued. The change was effected in the midst of the cholera epidemic; six days afterward the disease suddenly ceased. Typhoid fever too no longer attacks the convicts, and the death rate has declined to an extraordinary extent. It is, I think, impossible to avoid the conclusion that the exciting cause of dysentery in Millbank prison was the Thames water, and in all probability the noxious ingredient was derived from the sewage contained in it." Fecal contamination is undoubtedly the explanation of the excessive prevalence of dysentery in military camps in times of war. The notorious difficulty is a proper disposal of the excrement of large bodies of men; its indiscriminate deposit upon the ground from whence it could be washed by every rain into the shallow wells, springs, and creeks which afforded the water supply furnishes the key to the situation.

Contagium.—The question of the contagiousness of dysentery is one which has been extensively discussed. It would be useless to quote authorities or recapitulate the reasons they give for their opinions upon this subject. We can understand the wide differences which prevail when we consider the various standpoints from which the disease is viewed, and the want of unanimity as to what constitutes contagiousness. If we accept the modern definition of contagion—that is to say, when the micro-organism which causes a disease may under the ordinary conditions of life be freed from the body of the diseased person and by whatever means conveyed to the body of another in a condition capable of lighting up the disease anew—then we must conclude that dysentery is contagious, the evidence going to show that the contagium is in the dejecta, and is likely to reproduce the disease in other victims chiefly through the drinking water. It is probable that in the future we must recognize a number of different organisms as the cause of the various forms of dysentery, for it is impossible that conditions so varying in both their anatomical and clinical aspects as are the various forms of dysentery can be due to a single organism or even a single group of organisms.

The Amœba Dysenterica.—Although earlier observers had discovered certain organisms belonging to the protozoa in the stools, the first account given of the presence of amœbæ in the intestinal contents was given by Lambl in 1859. Lösch was the first author who gave an accurate description of a species of amœbæ which he found in the stools of a dysenteric patient, together with a careful clinical history and account of the autopsy. The first case studied by Lösch was received in the clinic of Prof. Eichwald in St. Petersburg in November, 1873. The amœbæ found in the stools were oval, pear-shaped or irregular in form, five to eight times the size of a red blood corpuscle. They were formed of an outer hyaline or faintly granular material enclosing a more granular mass. They were often so abundant that a single field of the microscope contained sixty or seventy. They changed their form frequently with great rapidity, thrusting out blunt processes which were at times quickly withdrawn; at others the granular interior slowly flowed into them and a change of place resulted. The nucleus was pale, of delicate contour, and difficult to make out. It always contained a nucleolus of variable size.

In the resting amœbæ the nucleus was always in the midst of the granular interior. Refractive vacuoles of various sizes which underwent some change of form were very numerous in the central mass. Foreign substances, such as bacteria, fragments of cells, and red blood corpuscles, were frequently seen in the amœbæ.

Cunningham, the only observer who has reported on the subject from India, states that he has found amœbæ in the intestinal canal of healthy persons, as well as in those affected with cholera and other diseases. He thinks the conditions which especially favor their presence are fluidity of the stools and an alkaline reaction. He found them also in the dung of horses and cows, and discovered bodies which he regarded as their spores.

In the cholera report of Koch an account is given of autopsies made on 5 cases of dysentery in Egypt. In the colon of most of the cases there were œdema and extensive ulceration of the mucous membrane; amœbæ were found at the base of the ulcers and in the material covering them in all but one case, and in that the ulcers were healed.

Amœbæ have been found in the intestinal contents by four Italian observers—Grassi, Perroncito, Calandruccio, and Blanchard. Their reports have reference only to the presence of the organisms.

Next in importance to the paper of Lösch on the amœbæ were the observations published in a series of papers by Kartulis of Alexandria, Egypt, on dysentery and abscess of the liver in 1887, 1889, 1890, 1891. In his first publication he gives a description of the amœbæ not differing materially from that of Lösch, except as to the size of the organism. The second paper, published in *Virchow's Archiv*, is devoted to the study of the relation of the amœbæ to abscess of the liver, and of his attempts to secure pure cultures. In another article he calls attention to the wider distribution of the amœbæ, and cites cases in which they were found in Greece. In his last article he gives details of his experiments in the cultivation of the amœba, and bespeaks for this organism as the cause of dysentery a greater recognition among pathologists than it has hitherto had.

The culture medium found most suitable was an alkaline straw infusion, to which was added either contents of liver abscess or stools containing amœbæ. In twenty-four to forty-eight hours a thin membrane formed on the surface which consisted of bacteria and young amœbæ. Studied in drop cultures, the amœbæ were much smaller than those in the stools; their movements in the swarm form were very active, but they did not send out pseudopodia. Among the actively moving amœbæ were found round inactive bodies with a nucleus and finely granular protoplasm about the size of a white blood corpuscle; these were thought to be spores.

Pure cultures were difficult to obtain: success was secured only in one case, where the material was obtained from a liver abscess free from bacteria. With both pure and impure cultures inoculations were made in cats with positive results, by injecting the cultures into the rectum and tying the anus. Feeding the animals with amœbæ gave negative results.

Hlava, in 1887, investigated the dysentery prevalent in Prague, and found amœbæ in 60 cases of partly endemic and partly sporadic dysentery. His description of them agrees fully with that of Kartulis. Hlava also injected stools containing the organisms into the rectum of dogs and cats, with positive results. Kartulis remarks that dogs in Egypt were spontaneously affected with dysentery, and the same amœbæ were found in the stools as in man.

Osler, in 1890, was the first in America to discover amœbæ, finding them in the contents of a liver abscess in a patient operated on by Dr. Tiffany of Baltimore. They were present in large numbers in the pus, and subsequently found in the stools. The patient had contracted chronic dysentery in Panama.

The organism, as described by Osler, conforms in every respect to the description of Kartulis except in being a little larger. In 1890, Musser and Stengel each reported 3 cases of dysentery in which amœbæ were found. In April, 1891, Dock gave a résumé of the subject, and reported 12 cases of amœbic dysentery occurring in Galveston, Texas. In 4 of these there was abscess of the liver, and in 4 this disease was only recognized at the autopsy, symptoms of dysentery not being present during life, the lesions in these cases involving only the cæcum. Dock's description of the organisms is in accord with that of Kartulis and others.

In 1891[1] Councilman and Lafleur reviewed the literature of amœbic dysentery, and gave the results of a careful analysis and study of 15 cases occurring in Baltimore, and a comparison of the symptoms observed in the catarrhal and diphtheritic forms with those of amœbic dysentery. As more than half of these cases were fatal, they were able to make many valuable additions to our knowledge of the pathological anatomy of this disease. In the remarks here given I have freely drawn upon the excellent summary of the subject as presented by these authors.

In September, 1893, the writer reported 7 cases of dysentery treated in the John Sealy Hospital, Galveston, Texas, during the previous year, in which the amœbæ were found. The symptoms in these cases were uniform and characteristic: as they all recovered or were discharged uncured, no autopsies were made. In 1 case the discovery of amœbæ in the pus from a liver abscess led to the diagnosis, the intestinal symptoms being very obscure. The organisms in these cases presented the features as recorded by other observers.

Baumgarten, speaking of the opinion expressed by Kartulis that the amœbæ are the cause of dysentery, says: "We regard it is improbable that the amœbæ can produce the entire series of changes which constitute the dysenteric process. Anatomically, dysentery consists in a combination of diphtheritic and purulent inflammation, which rapidly produces deep ulcerations of the parts affected; there is no analogy to make us believe that amœbæ can be the cause of the ulceration. We think it more probable that pyogenic micro-organisms play an important part with the amœbæ in the production of tropical dysentery."

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[1] *Johns Hopkins Hospital Reports*, vol. ii. Nos. 7–9.

Councilman and Lafleur, after an exhaustive study of the subject, state, as a part of their conclusions, "that the amœbic is a form of dysentery which etiologically, clinically, and anatomically should be regarded as a distinct disease, and that the amœba has been shown to be the causative agent from its constant presence in the stools and the anatomical lesions, and from the inoculation experiments of Kartulis."

While I am strongly inclined to believe in the correctness of this conclusion, yet, on account of the difficulty of obtaining pure cultures of the amœbæ, and the uncertainty of the inoculation experiments of Kartulis, the pathogenic influence of these organisms must be considered as lacking that complete and stringent proof requisite to identify its positive causative influence.

1. Acute Catarrhal Dysentery.

Pathological Anatomy.—Since acute catarrhal dysentery most frequently ends in recovery, opportunities for post-mortem examinations are rare in uncomplicated cases.

The colon, and more particularly the cæcum, hepatic, splenic, and sigmoid flexures, and rectum, are the parts chiefly involved, though sometimes the ileum is also affected. Areas of mucous membrane are congested, red, swollen, and more or less covered with tenacious, yellowish or brownish red mucus, with some admixture of pus. Punctate or diffused extravasations of blood are usually visible. The solitary glands are generally enlarged, and project as grayish white elevations, from the size of a pinhead to that of a pea. The submucous tissue is swollen from congestion and serous infiltration. If the case is prolonged, follicular ulceration or diphtheritic inflammation may ensue.

The following is a synopsis of changes as found in the intestines of a typical case reported by Councilman and Lafleur: "The patient, aged sixty-three, had dysentery two weeks before death. He had severe pain: the stools were fluid, but contained no blood. Numerous ulcers were found in the colon, especially the descending portion, and the rectum. The ulcers were usually superficial, and many confined to the mucous membrane; others were deeper, but none extended to the muscular coat. Some of the ulcers were round; others of irregular shape from the union of adjacent ones. The edges were smooth and were undermined. The intestine was not thickened, except about the largest and deepest ulcers. The mucous membrane generally was pale and soft. The tissues, after hardening in alcohol and submission to microscopic examination, showed decided changes. The superficial portions of the mucous membrane near the ulcers was broken down into a granular looking mass, in which only the remains of cells were found. Deeper down there was a diffuse infiltration with pus cells, most marked just above the muscularis mucosa. Lieberkühn's glands showed various stages of disorganization. In some instances they were dilated into thin-walled cysts, filled with pus cells; in others the cells were separated from each other, forming irregular masses of epithelium; the cells were generally swollen and with indistinct outlines. The lymphoid cells were increased and the solitary follicles slightly enlarged.

"In the mucous membrane corresponding to the whitish areas there

DESCRIPTION OF PLATE III.

FIG. 1: A transverse section of colon near the cæcum in a case of secondary diphtheritic dysentery following the amœbic form, complicated by an extensive abscess of the right lobe of the liver. Following is a brief history of the case: Aug. Schmidt, aged forty-three, native of Germany, laborer, admitted to Sealy Hospital, Galveston, Oct. 23, 1895. Lived in Galveston fifteen years; previous health good, with exception of an attack of diarrhœa fifteen years ago. Gave a history of diarrhœa alternating with constipation, lasting about three weeks prior to admission. Stools varied in number from four to ten daily; contained mucus, but no blood. There had been some abdominal pain, but no tenesmus. Condition on admission: anorexia, tongue thickly coated and brown, slight tenderness over right hypochondrium. Bowels obstinately constipated from Oct. 23d until Dec. 3d; stools averaged one daily. Under the use of repeated laxatives during the succeeding three weeks the number averaged two daily; enemata and purgatives were required to keep the bowels active during this time. Dec. 27th a severe uncontrollable diarrhœa ensued, the number of stools varying from three to twenty-three daily; the dejections were large, thin, and watery, containing mucus, small particles of fecal matter, and undigested food, chiefly casein; examination for amœbæ negative. Diarrhœa lasted until the patient died, Jan. 8, 1895. During the first four weeks the temperature varied from normal to 100.4° F.; the following three weeks it was higher, ranging from 100° to 102°, once reaching 103° F.; on Nov. 30th and Dec. 3d it was subnormal (97°). On Dec. 11th there was a severe rigor, followed by a temperature of 106.8 F.; similar rigors and high temperature occurred on the 14th, 19th, 25th, and subsequently. During this period the patient complained of severe pain in the hepatic region. Abscess of the liver was suspected, and an operation arranged for, but being postponed for some reason and the condition becoming hopeless, incision was abandoned. The autopsy revealed extensive ulceration throughout the large intestine, as shown by photograph. The drawing, by Prof. W. Keiler, made shortly after death, shows the dark discoloration, the oval-shaped ulcers, crowded together and mostly covered by a closely adherent diphtheritic exudation, extending in depth to the muscular coat, and having their long diameter across the gut. The drawing is life-size and the coloring true. The ulcers were situated mainly upon the crests of the folds of the mucosa, the grayish, dark green discolorations corresponding to the depressions between the folds. The entire colon was thickened and softened; the latter probably was a post-mortem change. The small intestines were normal. The entire right lobe of the liver was occupied by an abscess, in the contents of which amœbæ were found; there were no other important lesions. The case is one of great interest, as showing the insidious nature of amœbic dysentery—that unhealed ulcers may exist with obstinate constipation, and death finally occur from hepatic abscess or the intervention of an acute secondary diphtheritic ulceration of the intestine of such an extent and severity as to preclude the possibility of recovery.

FIG. 2: *a*, amœbæ coli of various sizes and shapes; *a′*, amœba coli, with especially delicate and numerous pseudopodia; *b*, elastic tissue remnants; *c*, crystals of hæmatoidin; *d*, phosphoric crystals; *e*, bismuth crystals; *f*, crystals of the fatty acids in combination with magnesium and calcium; *g*, spiral ducts of plant; *h*, spindle shaped trochid of plant; *i*, red blood cells; *j*, mucus not stained by bile; *k*, various epithelial cells of a yellow hue from bile; *l*, pus corpuscles stained by bile; *m*, various masses of mucus and animal débris stained by bile; *n*, partially disintegrated muscle fibres from meat diet.

The granular matter forming the bulk of the stool consists of animal and vegetable débris and bacteria, oil globules, etc.

PLATE III.

FIG. 1.

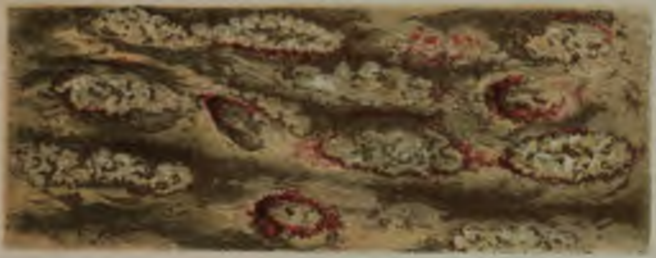


FIG. 2.

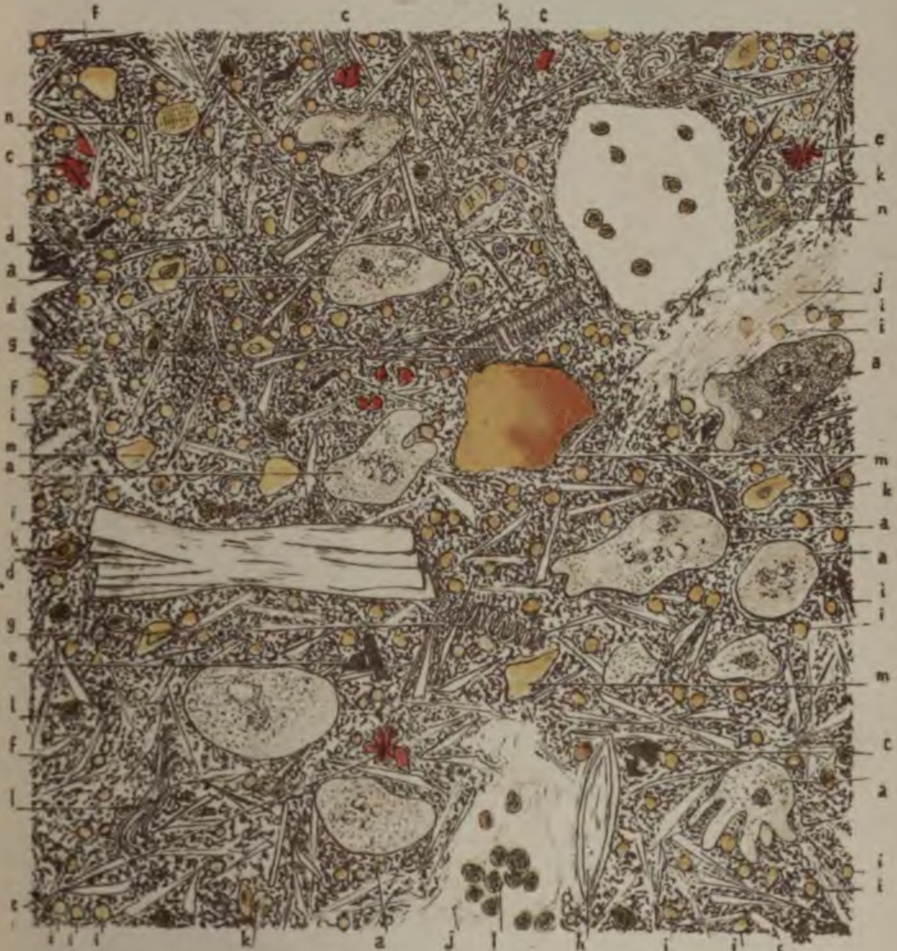


Fig. 1. Transverse Section of Colon near the Cæcum, in a Case of Secondary Dysentery following the Amœbic Form.

Fig. 2. Amœbæ Coli of various sizes and shapes.

(Drawing by Prof. A. J. Smith, University of Texas, Galveston.)

was a diffuse suppuration of the tissues. The glands were broken down, their confines lost, and they were represented by irregular masses of epithelium surrounded by pus cells. The ulceration extended through the muscularis mucosa, sometimes in only very small areas; at others the entire ulcer was seated in the submucosa. In such instances the submucous tissue was somewhat thickened, and the edge of the ulcer marked by granulation and pus cells. The pus cells extended deeply into the submucous tissue, sometimes diffusely infiltrating it, at others collecting in groups.

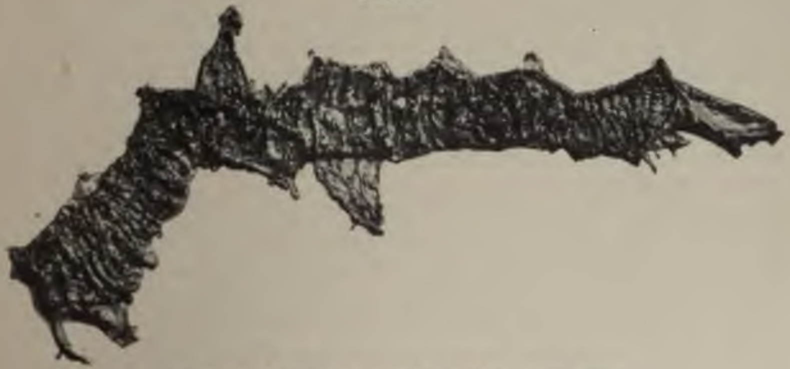
"Around the vessels everywhere there were dense accumulations of cells, swollen connective tissue corpuscles, and pus cells. A marked feature was the very great swelling of the connective tissue cells near the ulcers. They were converted into large, irregularly shaped masses, with a large vesicular nucleus. Scattered through the swollen connective tissue were numerous masses of fibrin. The vessels showed an increase in number and swelling of the endothelial cells; their walls were thickened and contained numerous pus cells, as did also the lumen."

As shown from this description, the lesions in catarrhal dysentery consist essentially in a suppurative inflammation of the mucous membrane, whence it is liable to extend into the deeper tissues.

2. DIPHTHERITIC DYSENTERY.

PATHOLOGICAL ANATOMY.—It is stated by Woodward that the majority of fatal cases of acute dysentery in which autopsies were made during the American Civil War were those in which diphtheritic inflammation was the characteristic morbid process. Similar lesions have been described by English writers in India, the French in Algeria, by English, German, and Irish observers in those countries, as by Woodward and others in America (Fig. 35 and Plate III. Fig. 1).

FIG. 35.



Photograph of colon (description of Case, page 348).

It appears to be certain that the lesions of most of the epidemics of dysentery are those of diphtheritic colitis, and, while diphtheritic inflammation may complicate the catarrhal and amœbic varieties, it is to be regarded as a distinct form. In fact, most cases of diphtheritic dysentery are found to be associated with catarrhal inflammation of other portions of the intestines, and this catarrhal inflammation is sometimes limited to the colon, but more frequently involves the lower portion of the ileum or may appear in detached patches higher up in the small intestines.

The diphtheritic process, which in most instances is to be regarded as having supervened upon the catarrhal inflammation, varies greatly in extent and as to the firmness and tenacity of the exudation depending upon the stage of the process in which death occurred. The exudation is sometimes limited to the descending colon and rectum, or to the latter alone; sometimes it involves other portions of the large intestine, or the whole of it, extending in some instances into the small intestine; the exudation is in some cases quite superficial, lying as a separable layer upon the mucous membrane, involving the outer epithelium and filling the follicles of Lieberkühn. Usually, however, in portions of the affected area a part or even the whole of the submucosa is also involved.

The exudation presents under the microscope the characteristics of any other croupous exudation, showing a finely granular or indistinct fibrillated appearance, which coagulates with various degrees of firmness, and entangles in the coagulum a variable number of white blood corpuscles. The parts embraced in the exudation promptly undergo coagulation necrosis, the depth of the slough depending upon the depth of the previous inflammation.

The exudation and resulting sloughs are primarily whitish or yellowish in color, or are often reddened by hemorrhage or colored greenish or black by subsequent changes in the blood. The loss of substance produced by separation of diphtheritic sloughs constitutes a form of dysenteric ulceration. The ulcers are of different sizes, and vary from mere abrasions to deep excavations that expose or even invade the muscular coat.

Death often ensues before sloughing is completed, the ulcers presenting no indications of the separation process: when the area destroyed is not too extensive, the ulcers may cicatrize and recovery take place, or more frequently remain in an indolent condition, a chronic flux persisting, which after a variable period proves ultimately fatal.

In some instances the ulcers may perforate the serous coat, death rapidly resulting from peritonitis. It is an important pathological fact of great significance in connection with the prognosis that very extensive ulcers from diphtheritic sloughing may completely cicatrize and recovery occur. The cicatrices are more or less puckered, and in rare cases stricture of the bowel may result from this circumstance.

In the early stages of the diphtheritic process the changes observed in perpendicular sections do not materially differ from those in catarrhal inflammation, except that the surface of the affected part is coated with a thin diphtheritic layer. This layer consists essentially of the blood fibrin, which begins to transude as soon as the inflammation is sufficiently intense. The behavior of the fibrin varies in accordance with its quality and the activity with which it is poured out. It may present almost any degree of firmness, from a jelly-like layer of very slight cohesion to a tough, firmly adherent mass, which can be strictly called a pseudomembrane, entangled in the substance of which are variously lymphoid elements (white blood corpuscles, pus corpuscles, and red blood cells): the latter especially are prone to accumulate near the mucous surface.

This fibrinous layer not only forms a coating of variable thickness upon the surface of the mucous membrane, but distends the glands of Lieberkühn, and there is an increased number of lymphoid elements in the adenoid tissue of the mucosa, the closed follicles, and the submucous connective tissue, thus ensuring more or less thickening of the intestinal wall.

In the graver forms of the diphtheritic process the capillaries of the mucosa are distended with blood, and hemorrhagic areas of considerable size are noted upon the superficial parts of the mucous membrane and in the deeper parts of the diphtheritic layer. In proportion to the increasing severity of the case the lymphoid elements infiltrate the submucous tissue, and a granular material similar to the surface exudation makes its appearance in the lymph spaces. Sooner or later during the progress of these alterations sloughing sets in, just as it does in diphtheria of the pharynx. The stage at which sloughing begins varies in different cases: in some the tissues retain their vitality until the mucous surface is coated with a dense yellow pseudo-membrane; in others at an early period the affected parts are swollen by a rich albuminous exudation containing only a moderate amount of fibrin and cell elements, in which sloughing may occur with great rapidity and destructiveness. This necrosis is rapidly followed by putrefactive changes in the dead parts, which condition is favored by the moisture and high temperature of the interior of the body.

Putrefaction is manifested microscopically by a granular metamorphosis of all the tissue elements involved into an unrecognizable mass of molecular débris. If the patient survives the occurrence of tissue necrosis, the sloughs separate by the ordinary suppurative process taking place adjacent to the boundaries of the necrosed portions. The depth of the primary diphtheritic ulcer depends upon the depth of the diphtheritic infiltration. The original ulcer may, however, extend both in area and depth, either by secondary sloughing or a true ulcerative process, the cell elements floating off as pus corpuscles; thus the muscular coat may be gradually involved and perforation rapidly take place by rupture of the thin tissue forming the floor of the ulcer.

3. AMŒBIC DYSENTERY.

PATHOLOGICAL ANATOMY.—The large intestine is chiefly involved, for the reason that here the amœbæ find favorable conditions for their development; the small intestine seems to be affected only when there is an enormous number in the colon, from whence they pass into the ileum. The most striking characteristic noticeable in all cases of this special anatomical form of dysentery is the great thickening of the intestine. In some cases thickening involves all the coats; in all cases it is more marked in the submucous coat, and in some confined in the latter. There is not only a general thickening due to œdema, but circumscribed thickenings are present, containing small cavities filled with gelatinous pus. These cavities communicate with the mucous membrane by a small opening. There are also various tracts communicating with neighboring cavities. (Plates IV. and V.)

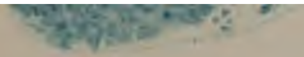
The elevated nodules vary in size: the openings often are no larger than a pinhead, or so large that the cavity is freely exposed; even then the surrounding mucous membrane is deeply undermined, and there are often sinuses in the submucosa leading off from the ulcers. The latter contain the same gelatinous looking material as the cavities, which, examined under the microscope fresh, show numbers of amœbæ, large round cells, red corpuscles, and pus cells.

Moving amœbæ are almost always found if the examination is made soon enough after death. The undermined ulcer in connection with the formation of cavities and various tracts in the submucosa appears to be the variety oftenest observed, though other forms of ulcers may be present in the same intestine—*e. g.* when the undermined edges have sloughed away, leaving the edges smooth in places and in others only slightly undermined. These ulcers are most frequently met with in the last portion of the transverse and descending colon. The submucous coat is the one chiefly affected; it is infiltrated and œdematous, not only at the site of the ulcers, but elsewhere.

The ulcers increase by gradual infiltration and softening of the tissues, with subsequent necrosis of the overlying structures. The roof covering in the more or less closed ulcer, the softening continues at the sides, and an ulcer with undermined ragged edges is found. The base of such ulcers is usually clean and is formed by the muscular coat; the latter, while it offers a barrier to molecular disintegration, may also become necrotic by gradual infiltration along the connective tissue septa until the subserous coat is reached. During the continuance of this process the peritoneum becomes greatly thickened and involved in a similar destruction.

The mucous membrane seems to suffer least, or rather the lesions in this coat are secondary to those of the submucosa, the process consisting essentially of advancing infiltration and softening in the submucous and intermuscular tissue, with subsequent necrosis of the overlying tissue. Reaction on the part of the tissue is shown in the formation of granulation tissue rather than of pus. When suppuration is a prominent feature in the process, it is due not to the action of the amœbæ, but to the pus organisms which enter the tissues. The amœbæ can extend in the tissue a considerable distance, which latter softens and breaks down, resulting in the formation of the large ulcers with soft undermined edges. Sometimes there is great undermining before breaking down of the overlying tissues, large sloughs thus resulting. In other cases the amœbæ are cast off with the softened tissue, leaving an ulcer with smooth sides and base, or the suppuration of the tissues produced by bacteria may get the upper hand and an ordinary suppurating ulcer result, the amœbæ being either cast out by the purulent softening or possibly destroyed by pus products or bacteria, there appearing to be an antagonism between the amœbæ and the suppuration process.

Councilman and Lafleur (to whose excellent description of the lesions of this form of dysentery the writer is indebted, and the reader is referred for fuller details) state that, while the lesions of amœbic dysen-



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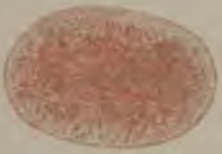

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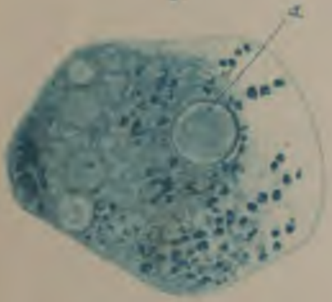

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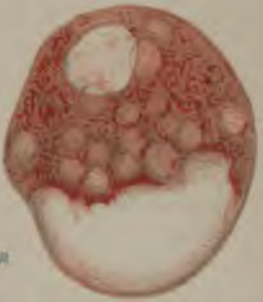

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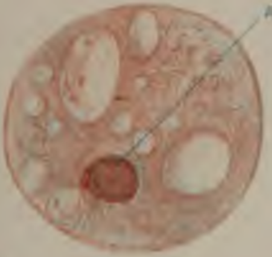

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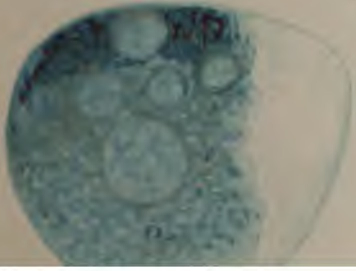

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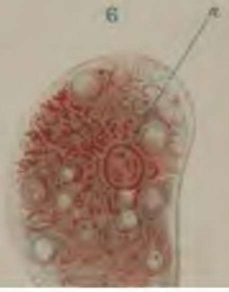
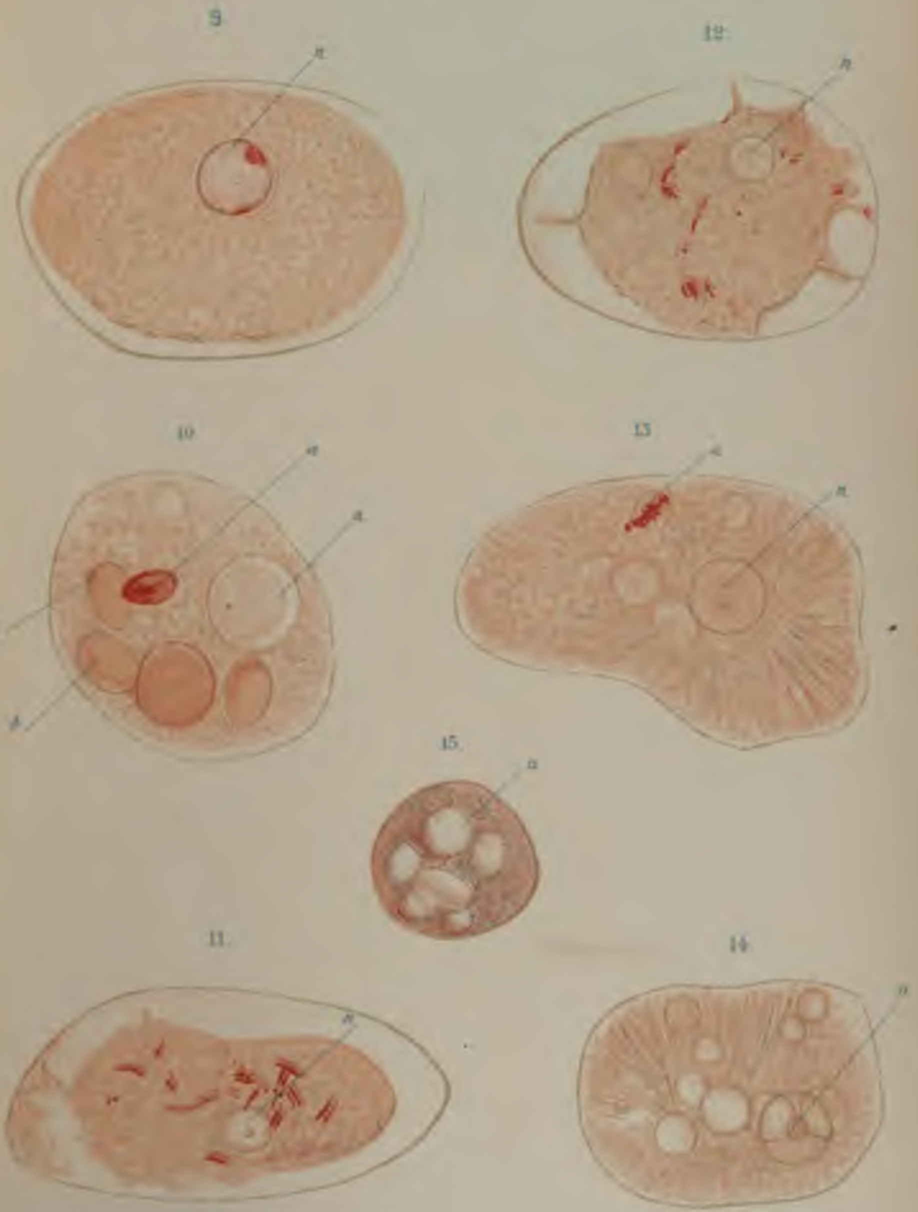


PLATE V.



Dysenteric Amœbæ.

Figs. 9, 10, 11, 12, 13, and 14 are from various tissues hardened in Flemming's solution.

In Figs. 9, 11, and 12 the central mass has shrunken from the periphery. In Figs. 11 and 12, nuclear detritus in the form of small brightly staining rods is seen. In Figs. 13 and 14 are the radiate-like structures described in the text. In Figs. 10 and 13 are portions of the nuclei of included cells. In Fig. 10 there are included blood-corpuscles.

(Councilman and Lafleur, *Johns Hopkins Hospital Reports*, vol. ii. Plate VII.)

tery conform most closely to the description which has been given of follicular colitis, they found the follicles involved in only one out of eight cases, and then it was a passive process and in no case originating in the follicles.

Abscess of the Liver.—As illustrating the frequency of this lesion in amœbic dysentery, the following facts are significant: Of the 12 cases reported by Dock, 5 died, and in 4 there was abscess of the liver; in Councilman and Lafleur's series of 15 cases 8 died, and of these 6 were complicated by hepatic abscess; of the 7 reported by the writer, none of which were fatal, 1 had abscess of the liver. Thus, out of 34 cases 11 were subject to this complication, and of 13 fatal cases 10 had abscess of the liver. These figures are confirmatory of the opinion that the amœbic is the prevalent form of tropical dysentery, for we find (not quoting authorities or details) that in India, Cochin China, Algeria, and Egypt hepatic abscess is discovered in 1 out of about 4 fatal cases; also that in Cuba, Brazil, Chili, Venezuela, and Mexico liver abscess is of great frequency in connection with dysentery.

Not discussing here the causes or modus operandi of liver complications, we proceed with the anatomical changes found in this organ. The commonest seat of abscess is the right lobe and its lower border, corresponding to the hepatic flexure of the colon or the upper surface close to the suspensory ligament. In the last situation the abscess usually extends through the diaphragm into the lung.

The forms of liver abscess can be divided into (*a*) the small very acute variety, (*b*) the larger one with partially fibrous walls, and (*c*) the chronic abscess with hard, dense fibrous walls. The microscopic character of the abscess contents varies. The smaller contains a viscid translucent liquid with a few pus or lymphoid cells, fatty granular material, fragments of distorted liver cells, a few red blood corpuscles, and numerous amœbæ in active motion. In the large abscess the fluid is not so clear; its opacity is not due to pus cells, but to fat, fragments of tissue, and broken-down liver cells. The fluid cannot properly be called pus, as there is a remarkable absence of well preserved cells. Amœbæ are found scattered abundantly through the contents of the abscess, especially at its periphery and in the included portal tissue. At the edges they are found chiefly in the capillaries, and usually do not extend in the tissues beyond the area of necrosis.

Some abscesses are of microscopic size, and are not connected with the larger ones: in these we find the same process of destruction and extension as in the larger ones. Abscess formation is not the only change, for there is found also a more or less extensive necrosis of liver cells around the centre veins which does not appear to be due to the presence of amœbæ. These organisms invade the already necrotic tissue, and appear to influence its breaking down and liquefaction. While the more chronic abscesses differ from the acute in many respects, they have most features in common, and the differences can be explained probably by the smaller number and less intense action of the amœbæ and a minor degree of diffuse necrosis of the tissues.

There are certain abscesses showing a combination between those with fibrous walls and the small ones of recent formation. In these, portions of the walls are distinctly fibrous and other portions are forme by necrotic tissue, which extends also into the surrounding liver tissue. Occasionally in the vicinity are small necrotic foci with central softening which are isolated from the large abscesses, but become connected with it by a gradual increase in size and continuation of the softening process in both directions. Thus the chronic abscesses increase in size in two ways—first, by gradual extension with a continual new formation of fibrous tissues, and secondly, by formation of separate small abscesses which soon become a part of the larger.

The smaller peripheral foci may meet, and in this way cut off larger or smaller areas of tissue. The irregularity in the walls of the large abscesses is produced in this way. The amœbæ are not relatively so numerous in the large as in the small abscesses; often in large sections they are not found at all. They are usually to be seen in the necrotic edges of the abscess and in the small foci adjoining.

Summing up the changes in the liver it appears that there are two classes of lesions: First, extensive necrosis of tissue which does not appear to be due to the direct action of the amœbæ, for the organisms are not found in them, and they are too regular in situation and extent for such production. These necrotic lesions seem to be due to the action of the soluble chemical products of the amœbæ absorbed from the intestinal ulcers. Second, abscess formations which we are justified in believing are due to the direct action of the amœbæ for the following reasons: They are invariably found in every abscess; they are most numerous in the smallest and most recent, and in the situations where the abscess was extending; no other organisms are found in the smaller abscesses; the few bacteria found in the large ones do not appear to have any causal connection; none of the pus-producing organisms are found; and, finally, the lesions are of a different character from those produced by bacteria.

Abscess of the Lungs.—Abscess in these organs secondary to abscess on the upper surface of the liver was found in 3 out of 6 cases by Councilman and Lafleur, who observed the following: Abscesses of the lung resembling those of the liver in several particulars. They were lined with opaque, ragged necrotic material, which in places projected in large masses into the cavity. There were also projections from the abscess into the surrounding pulmonary tissues, and by union of these large masses of tissue were cut off, as in large hepatic abscesses. In a few places the abscess wall was comparatively smooth and formed of dense connective tissue. In other places there was no definite boundary between the necrotic tissue lining the abscess and the surrounding lung tissue. These abscesses were usually empty. Examination microscopically of the contents clinging to the wall showed granular detritus, round lymphoid cells, a few pus cells, numbers of red blood corpuscles, fat globules, and amœbæ; also elastic fibres of pulmonary tissue.

The lung tissue in the vicinity of the abscess showed the alveoli to be small, and an enormous increase of the interstitial connective tissue was noted. The bronchi were also altered: their walls were thickened, containing great numbers of round cells; some were filled with fibrin and pus cells, while in nearly all of them a similar condition to that of the alveoli was found in the projection of masses of connective tissue from the wall.

The amœbæ varied in numbers in different cases and in different parts of the same abscess; they were especially numerous in places where the abscess was rapidly advancing, and where there was no distinct wall; they were also numerous in the tissues around the abscess, decreasing as the distance from the abscess increased. They were also found in the wall, epithelium, and lumen of the bronchi near the abscess.

In the production of both lung and liver abscess the action of the amœbæ is similar: they act by causing a necrosis and liquefaction of the tissue; the peculiarity of their action and the difference which distinguishes these effects from those of bacteria consist in the general absence of acute inflammatory reaction on the part of the surrounding tissues. In all cases, in the intestines, liver, and lungs, unless there is a complication in the presence of pus-producing bacteria, there is an absence of suppuration. The extension of the lung abscess into the surrounding tissue is probably due to the entry of the amœbæ by means of bronchi bordering on the abscess.

It is highly probable that the amœbæ reach the large intestine chiefly through the drinking water: food is less likely to be the source of infection, as the organisms would be destroyed in the process of cooking. No action is exerted by them upon the stomach or small intestine, as they do not find here suitable conditions for their increase, but in the colon, finding a favorable soil, they multiply rapidly, and, aside from the production of definite ulceration, we have evidence of their causing a superficial necrosis and softening of the epithelium, an increased secretion of mucus from the epithelial cells, and cysts of the mucous membrane from the dilatation of glands whose mouths have been plugged from the accumulation of mucus.

The question arises as to the routes by which hepatic and pulmonary metastases take place. The evidence seems to show that in most instances the amœbæ reach the liver by passing through the intestine, entering the organ directly from the hepatic flexure of the colon, or, wandering along the upper surface of the liver in the abdominal cavity beneath the diaphragm they may cause peritonitis, or, as is more likely, produce no effect upon the peritoneum. There may be infection through the bloodvessels also, as shown in cases where there is formation of small multiple abscesses both on the surface and through the liver tissue.

Abscess of the lung appears to result from a direct extension through the diaphragm from the liver, as it is usually found in that portion of the lower lobe of the right lung which is in contact with the diaphragm.

4. SECONDARY DYSENTERY.

PATHOLOGICAL ANATOMY.—The lesions of this form of dysentery are usually those of diphtheritic colitis, previously described. In some cases there may be only a thin superficial infiltration of the upper layer of the mucosa in localized regions, especially along the ridges and folds of the colon, often extending into the ileum. In severe forms the entire mucosa may be involved and necrotic, often having a rough granular appearance. In that form which occurs in connection with pneumonia the exudation may consist of a firm white pellicle which seems to lie upon, and not within, the mucous membrane.

Follicular Ulceration.—A great deal has been written, especially by older authorities, upon the subject of follicular dysentery. A careful study of the results of autopsies and comparison of the clinical histories will show that the lesions in a majority of these cases correspond to the description of amœbic dysentery as herein given.

In the cases cited by Woodward as acute or "Chickahominy diarrhœa" he thus describes the lesions: "In some of the fatal cases of acute diarrhœa the only intestinal lesion observable with the naked eye was a reddish discoloration of the mucous membrane, which for the most part occurred in patches of various dimensions from a few inches to several feet in length. Such patches were observed in all parts of the intestinal canal, but were more common in the ileum than in the jejunum, and were still more frequent in the colon, where they particularly affected the cæcum and sigmoid flexure. Microscopical examinations of these reddened patches showed their color to be due either to an engorgement of the small vessels with blood, to transudation of its coloring matter, or to actual hemorrhage into the mucous or submucous layer, or to a combination of these conditions. In the majority of cases the solitary follicles situated in the reddened patches were more or less enlarged; the most common condition being that in which they had attained the size of pinheads and appeared as whitish or yellowish elevations surrounded by a circlet of increased vascularity. In the colon these minute elevations were generally sessile; in the small intestine they often had constricted necks and projected from the surface of the mucous membrane.

The question arises, How many of these cases in which there is follicular inflammation proceed to ulceration, and how many which have been described as follicular ulceration are really such? It is natural, upon seeing enlarged follicles in certain cases and in others small nodular ulcers, to regard the latter as coming by gradual transition from the former. But, as we have seen in the amœbic form, ulceration does not begin in the follicles, and when they are affected it is only in common with the other tissues in the submucous coat.

Post-mortem Appearances in Chronic Dysentery.—Woodward divides the lesions of those dying from chronic fluxes into three groups, which may exist either singly or variously combined:

(1) Chronic inflammation of the mucous and submucous coats of the intestines, especially of the colon without ulceration.

(2) Chronic inflammation accompanied by follicular or other ulcers, especially in the large intestine; in these cases the pathological picture is often complicated by the development, just before the fatal issue, of diphtheritic inflammation between the ulcers.

(3) Extensive ulceration of the large intestine, the result of sloughing during a previous attack of acute diphtheritic dysentery.

To these three groups may be added a fourth—viz. (4) Catarrhal dysentery, becoming chronic and attended by a form of ulceration differing from the amœbic and diphtheritic.

(1) In the first group, chronic inflammation without ulceration, we find that the bright red discolorations of acute inflammation are replaced by mahogany red, brown, green, slate color, ash color, or other neutral tints of various hues. Black, bluish, or brownish deposits of pigment

are observed in the closed follicles or in patches scattered over the mucous membrane of both large and small intestines, and in the apices of the villi of the latter, especially of the ileum. With these modifications of color enlargement of the solitary follicles, and more or less thickening of the mucous membrane and submucous connective tissue, especially of the large intestine, are associated. The degree of this thickening varies with the duration and severity of the case.

(2) The second group of cases, including those of chronic inflammation accompanied by follicular or other ulcers, can be properly classified with the amœbic form. Confirmatory of this view, Councilman and Lafleur state that they examined the colon specimens in the Army Medical Museum at Washington, many of the specimens represented among the illustrations in Woodward's book, picking out those which seemed to represent the amœba forms, and on consulting the histories of the cases found in each a clinical history corresponding to amœbic dysentery.

The writer, who has had under observation a larger or smaller number of cases of chronic dysentery for the past twenty years in the hospitals of Galveston, is confident in the light of present knowledge that most of such cases belong to the amœbic variety.

(3) The third group of lesions in chronic dysentery are those where there is extensive ulceration of the large intestine succeeding an attack of the acute diphtheritic form. As a description of the morbid anatomy of such cases has already been given, it will be unnecessary to repeat it here.

(4) Ulceration following acute catarrhal dysentery has also been described. In these last two groups the patient is gradually exhausted by a long process of suppuration taking place from the unhealed ulcers, or is rapidly carried off by the supervention of an acute diphtheritic inflammation of the large intestine.

1. Acute Catarrhal Dysentery.

Symptoms and Clinical Course.—This form of dysentery often occurs during the progress of an ordinary acute diarrhœa after the latter has lasted a few days or weeks, or it begins as an independent affection, frequently coming on after more or less protracted constipation. In the latter event it is usually preceded by a sense of malaise, with uneasiness in the abdomen, resembling the sensations incident to indigestion. These are succeeded by abdominal griping, accompanied by a desire to go to stool. The dejections are at first feculent and copious, though not infrequently they are scanty, mucous, and without fecal admixture from the beginning. It is only in rare cases that this mild form of the disease begins with a rigor followed by fever, as is common in the diphtheritic form. When catarrhal dysentery supervenes upon diarrhœa the stools sometimes suddenly acquire the dysenteric characters; usually, however, the latter are gradually developed. These characteristics are as follows: At intervals griping abdominal pains occur, generally in the umbilical region, but often extending along the course of the ascending and descending colon, and accompanied by a dull pain in the loins. The pains resemble those of acute diarrhœa, but are usually more severe.

They are accompanied or followed by an urgent desire to expel the contents of the bowels, but the spasmodic efforts that ensue are only successful in expelling, after prolonged straining, a little mucus or mucopus, which may or may not be mixed with blood. This scanty discharge is not followed by the sense of relief which is noted after the discharge in acute diarrhœa, but painful sensations remain in the rectum and anus even after a lull has taken place in the repeated expulsive efforts. The term *tormina* has been long in use to describe the griping abdominal pains; the painful expulsive efforts are called *tenesmus*. The paroxysms of tormina and tenesmus vary in frequency according to the severity of the attack, from half-hourly, hourly, or longer intervals to every few minutes. In some instances they occur so often that the patient is hardly able to leave the closet. Notwithstanding the violence of these local symptoms, there is usually at first but little constitutional disturbance. The appetite is fair; there is no complaint of thirst; the pulse is but slightly increased in frequency; the temperature is normal; but usually there is a sense of weakness, causing the patient to prefer the recumbent posture. After a few days, however, there is more or less complete anorexia, coated tongue, nausea, sometimes vomiting and slight fever, the temperature rarely exceeding 100–101° F. The paroxysms of tormina and tenesmus are usually not so frequent in the morning hours, but increase in number during the afternoon and through the night. The pain and loss of sleep produce debility, restlessness, and other evidences of nervous disorders. The disease now may take one of these directions: (*a*) The symptoms may moderate and convalescence ensues; (*b*) they may become aggravated, and the case assumes the character of diphtheritic dysentery; or (*c*) they may persist with fluctuations of intensity and gradually pass into a chronic flux.

In the milder cases, which constitute the majority, convalescence begins about a week from the time the stools become distinctly dysenteric. As the case progresses toward recovery the paroxysms of tormina and tenesmus become less frequent and painful: the surest sign of approaching convalescence is the reappearance in the stools of fecal matter. The passage of hard fecal lumps (scybala) is not infrequent in the early stages, or they may occur subsequently from having been collected in the pouches of the colon without being of favorable import, but when the muco-purulent and bloody stools are replaced by those of a semifluid fecal character, we may expect a speedy recovery.

In the *American Journal of the Medical Sciences* for July, 1875, Austin Flint published an important contribution upon the natural history of acute dysentery, consisting of a report of 10 cases observed without medicinal treatment. From the analysis of these he concludes: (1) "The disease in a temperate latitude tends, without treatment, to recovery; (2) it is a self-limited disease, and its duration is but little, if at all, abridged by methods of treatment now and heretofore in vogue; (3) convalescence is as rapid when active measures of treatment have not been employed as in cases actively treated; (4) relapses do not occur in cases in which the disease has been allowed to pursue its own course without active treatment; (5) sporadic dysentery in a temperate climate does not eventuate in a chronic form of the disease." All of the 10 cases ended in recovery. The most protracted one lasted twenty-one days, of which fourteen were occupied by the preliminary diarrhœa. The shortest case lasted six days. The average duration, excluding the one with preliminary diarrhœa, was about ten days.

While these observations of Flint are of great value as showing the course of the disease when uninfluenced by treatment, and while it is doubtless true, as stated by George B. Wood, that in the vast majority of cases the disease takes this favorable turn, yet when a larger number of cases are observed it will be found that some, after running the course as above outlined for one or two weeks, pass into the diphtheritic form. Others without the latter complication are accompanied by severe symptoms of constitutional disturbance, from impaired digestion, rapid emaciation, exhaustion, and possibly death. Still other cases may gradually assume the characters of a chronic flux.

Vesical tenesmus and prolapsus ani may accompany simple catarrhal dysentery, but are less frequent and intense than in the diphtheritic form.

PROCTITIS.—Cases are not infrequent which present many of the symptoms as above outlined where the inflammatory process is limited to the rectum. Proctitis, as this condition is called, may be acute or chronic, and may depend upon a multitude of causes. The acute forms, as previously mentioned, may be due to dietetic errors. There are some persons in whom the rectum appears to be the *pars minoris resistentiæ*. Dysenteric symptoms in such individuals may follow the ingestion of articles of food which in others would be entirely innocuous, or irritant foods, which in most persons would be followed by a simple diarrhœa, in them produces a proctitis. Traumatic influences of various kinds play an important rôle. Among the more common of such causes are the presence of foreign bodies, impaction of fecal masses, intestinal parasites, abnormal sexual intercourse, careless use of instruments, etc. The condition is also often consecutive to other abnormal processes of the rectum and neighboring organs—*e. g.* hemorrhoids, polypoid growths, prolapsus, cancer, stricture, gonorrhœa, uterine and periuterine inflammation. The long continuance of any of these factors may result in chronic inflammation and ulceration of the rectum, as well as of suppuration in the perirectal tissues. The enumeration of these causes emphasizes the necessity in all cases, when the symptoms point to the rectum as the seat of the disease, of making a careful physical examination by touch and speculum, as a removal of the cause constitutes the most important indication for treatment, and is alone in many instances sufficient to effect a cure. As proctitis is fully described in special treatises, it is not necessary to enlarge upon the subject here.

2. DIPHTHERITIC DYSENTERY.

SYMPTOMS AND CLINICAL COURSE.—This form may begin in four different ways: 1. It may have been preceded by the symptoms as above described of a simple inflammatory dysentery. 2. In numerous cases it may be abruptly developed during the process of a chronic flux. 3. A primary diphtheritic dysentery may occur without having been preceded by any preliminary catarrhal stages. 4. It may occur in a secondary form after various acute and chronic diseases, with an absence of bowel symptoms or a diarrhœa consisting of three or four large movements during the day or perhaps the passage of a little blood and mucus. Those cases beginning as an acute catarrhal dysentery, instead of pursuing the ordinary course toward recovery, as above outlined, exhibit a more or less gradual aggravation of all of the symptoms. The patient grows more emaciated, becomes very weak, and eventually sinks into a condition of collapse, with cool surface and extremities and greatly enfeebled heart action. As the disease progresses the tongue becomes brown and dry or smooth, red, and dry, sometimes fissured; the anorexia and thirst become extreme; the abdomen tender to the touch and often distended with flatus; the skin is sallow or slightly jaundiced; the expression is anxious; the eyes appear sunken and acquire a vacant expression. *Pari passu* with these symptoms there is a change in the character of the stools, which at first consist of stringy mucus, more or less mingled with blood and pus, but now contain a quantity of yellowish or reddish masses of various sizes, which upon microscopic examination are seen to be necrosed particles of the diphtheritic exudation. The mucus or muco-pus of the stools is now mingled with a thin reddish serum, which sometimes entirely replaces it. In this fluid the pieces of necrosed membrane float, giving the passages the appearance of raw meat minced and mixed with bloody water. The stools have a characteristic cadaveric odor. About this time the skin around the anus is apt to become excoriated; prolapsus ani is likely to occur from the extreme tenesmus. The patient also complains of strangury and vesical tenesmus. The urine is generally decreased in amount, is of high color and specific gravity, and is occasionally albuminous.

Notwithstanding the extreme exhaustion, the patient often survives till the end of the second, third, or even fourth week from the commencement of the dysenteric symptoms. Death in the third or fourth week is apt to be the result in cases presenting the above-mentioned characteristics. Usually a few days before the fatal ending the stools become brownish or black and of a very offensive putrid odor; they also often contain larger fragments than before of necrosed mucous membrane, though this is not uniformly the case. Those cases which are not preceded by diarrhœa, but begin as dysentery from the first, pursue a similar course to that above sketched. Not infrequently they begin with a chill, followed by fever and the onset of the abdominal symptoms; the temperature is usually higher than in the type just described. Pronounced nervous symptoms are not unusual—headache, delirium, flushed dusky face, and subsultus tendinum. The fever passes into a typhoid form, with sordes upon the teeth, a rapid weak pulse, 110–140, and a continued high temperature. Those cases which begin with an active fever frequently pass into a condition of collapse, with slight elevation of temperature, cool surface, and a pulse which, though full, is but little accelerated or slower than usual.

When diphtheritic dysentery is developed during the progress of a chronic flux, it is apt to occur suddenly and prove rapidly fatal, the patient being already exhausted from the chronic disorder, and probably in a state of excessive emaciation. After some exposure to cold, intemperance in eating or drinking, and often without any assignable cause, the stools suddenly acquire the diphtheritic characters, accompanied by more or less fever, and rapidly followed by fatal collapse.

In the more protracted cases the disease pursues a less uniform course. There are periods of improvement succeeded by relapses at irregular intervals. During the time when the patient is better the stools are found to contain more or less fecal matter, semi-consistent, mixed with the blood, pus, and mucus. During the periods of aggravation feculent matter again disappears. Such cases may end in recovery in from one and a half to two months, may prove fatal, or pass into a chronic dysentery of indefinite duration. Convalescence is likely to be a tedious process in any event, and more so in proportion to the violence and duration of the disease and the extent of exhaustion of the patient's vitality. The bowels are left in a condition of extreme sensitiveness, when the slightest disturbing cause, as a trifling imprudence in diet, exercise, or changes in the weather, will bring on a relapse.

The clinical picture above outlined may be modified by various complications which are likely to occur, as malarial fever, scurvy, typhoid fever, or some intercurrent inflammation. These complications will be considered subsequently in detail.

3. AMŒBIC DYSENTERY.

SYMPTOMS AND CLINICAL COURSE.—This form of dysentery may be divided into four groups:

1. Comparatively mild cases;
2. Grave, gangrenous, or typhoid forms;
3. Chronic forms;
4. Masked forms.

It should, however, be borne in mind that this classification, which is essentially the same as propounded by Dutroulau and others, is purely arbitrary, and is introduced only to facilitate description. Cases will be observed to pass from one grade of severity to another. Mild cases may become severe or gangrenous; all forms are more or less disposed to become chronic.

Masked forms may have their true nature exposed by an explosion of dysenteric symptoms or be recognized only at the autopsy.

Amœbic dysentery is characterized by a variable mode of onset, an irregular course, marked by alternate intermissions, exacerbations, and a decided tendency to chronicity. The onset may be abrupt or gradual in the first instance: without premonition the patient is seized with colicky pains in the abdomen and diarrhœa; nausea and vomiting may or may not be present; in most cases there is no fever. The stools are frequent and watery; blood may or may not be present at first, but subsequently blood and mucus are both likely to be found. In some cases, after a variable period of slight ill health, a diarrhœa sets in, the stools are watery, contain more or less mucus; blood is either absent or only occasionally present.

There are a certain number of cases where the abdominal symptoms are either entirely absent or so obscure as to escape attention until perhaps the occurrence of hepatic or hepato-pulmonary abscess suggests the probability of amœbic dysentery. Illustrative of the comparative frequency of such instances is the fact noted by Dock, when out of 12 cases in only 6 was there a history of dysentery, in 2 it might have been elicited by careful examination; in 4 there was an entire absence of such history; in 2 the autopsies revealed the fact that the lesions were limited to the cæcum, which partly explained the absence of dysenteric symptoms. In one of the cases reported by the writer the discovery of a liver abscess containing amœbæ first led to the suspicion of dysentery. There are doubtless cases where, the intestinal lesions having healed, the disease can only be recognized by its sequelæ and complications.

The course of the disease is characterized in most instances by an irregularity in the dysenteric symptoms irrespective of the mode of onset. At irregular intervals there are intermissions, followed by exacerbations without apparent cause; the delusive hope is often entertained that the abatement of symptoms is the result of treatment, and that a genuine convalescence is at hand, when suddenly the stools acquire the dysenteric characteristics in such an aggravated way as to speedily dispel such delusions.

There are other cases, again, remarkably uniform and only marked by an obstinate looseness of the bowels: the condition hardly deserves to be called diarrhœa, as the stools are semi-consistent, perhaps containing no blood or only a little blood and mucus, the invariable presence of the amœbæ, however, showing the true nature of the disease. Even the gangrenous cases, while there are no actual intermissions, show periods of partial abatement followed by exacerbations. The tendency to chronicity is well marked in most cases; those complicated by extreme sloughing or a severe typhoid condition are the exceptions, and are apt to terminate by death in two or four weeks. The milder cases in Councilman and Lafleur's series show a wide range of duration, varying from six to thirteen weeks. Those coming under the writer's observation all assumed a chronic character, and those which recovered lasted from three to four months.

A clearer idea of the symptomatology of this form of dysentery will be obtained by presenting a brief analysis of its most important features.

General Condition.—The milder cases will be found in some such condition as follows: More or less muscular debility and emaciation, both varying in degree according to duration and severity. In the writer's series the loss of flesh was rapid and excessive. The mucous membranes are pale, decubitus indifferent. Expression dull, mind clear. Skin dry and sallow. Tongue pale and flabby, moist, and slightly furred. Abdomen of normal appearance or sometimes retracted. Temperature normal or only slightly elevated. Pulse 70 to 90. Respiration 18 to 30. More or less anorexia. Rest disturbed by disposition to evacuate the bowels. Graver cases show a modification of this clinical picture: the evidences of prostration are more marked; the face may be drawn, slightly cyanotic or flushed, and the expression anxious. The anorexia is increased; intense thirst and sleeplessness are apt to occur. The abdomen becomes retracted; there may be free sweating. The temperature may become subnormal, the pulse small and rapid, the respirations proportionately increased in frequency. In the chronic cases the progressive emaciation and anæmia are notable features, the skin in consequence becoming dry, harsh, and of a dull yellowish color. *Anæmia* has been noted by all observers; there is a deficiency both of corpuscles and hæmoglobin, which is due to a combination of causes—viz. continuous losses of blood and albumin, malnutrition, and destruction of red corpuscles by the amœbæ. *Diarrhœa* is the chief and in some instances the only feature of the disease. It varies greatly in character and in frequency of the stools according to the extent of the intestinal lesions, and at different times in the same case. The occurrence of intermissions and exacerbations as a special characteristic has already been noted. The exacerbations often begin suddenly and subside in the same way: they may last from one to ten days, becoming progressively worse and of longer duration in fatal cases. The intermissions show a wide range of duration, varying from one day to three weeks, during which time the stools are soft or even formed, but with more or less adherent mucus. The *stools* vary greatly in frequency, amount, and character, not only in accordance with the severity of the intestinal ulceration, but from day to day in individual cases. In the *gangrenous* form there may be as many as thirty or forty during twenty-four hours, subsequently declining to eight or twelve, and three or four toward the end in fatal cases. The amount expelled at each movement is at first small, and often consists of clear or turbid mucus, more or less mixed with blood and sometimes small fecal masses. As ulceration advances the dejections become more copious and watery; blood is less frequently observed, but small shreddy particles of grayish or light yellow color appear, mixed with blood-stained mucus. When extensive sloughing is occurring the stools are grayish, greenish, reddish-brown, or variegated in color, quite liquid or pultaceous, and have a very offensive odor. Mixed with finely divided shreddy mucus and streaks of dark blood are seen larger, tough, stringy masses of necrotic tissue. The stools are not distinctively purulent, but the slimy, gray, liquid dejections contain more pus cells than the others. In all the dejections there are found more or less numerous small opaque or translucent, gelatinous grayish yellow masses from 1 to 3 mm. in diameter. In cases of moderate severity and abrupt onset for a week or ten days the stools are similar to those at the beginning of gangrenous dysentery. If the onset has been gradual, liquid brownish yellow stools containing mucus, streaks of blood, and many of the gelatinous grayish masses are the rule. The number of such movements varies from four to ten in twenty-four hours, and a flux of this degree, but more irregular and without blood, may continue for weeks. During an exacerbation the stools increase in frequency, resembling those of the second period of the gangrenous form, sloughs being occasionally found and blood reappearing.

The stools in chronic cases have a more uniform and homogeneous appearance. They are watery or of the consistence of thin gruel, of an earthy or dull yellow color, and contain a few or many particles of clear mucus. During an exacerbation blood and pultaceous material may be seen; in intermissions of the diarrhœa the fæces are soft and pasty or partly formed, but mucus is persistently present. Particles of undigested milk and other food are often seen. The reaction of these stools is usually alkaline.

Microscopical Examination of Stools.—In the small, mucoid, and bloody stools of the acute stage there are found in varying proportions red blood cells. The *cercomonas intestinalis* is sometimes present. At a later period, in gangrenous cases and those of moderate severity, the cellular elements are less numerous, and float in a mixture of granular detritus and bacteria. Elastic tissue fibres are observed, but the necrotic masses are devoid of structural appearance. In the liquid grayish stools of the chronic forms recognizable elements are still fewer, making the detection of the amœbæ much easier.

Amœbæ are found in all varieties of these stools and at all periods of the disease. They vary in number in different cases and at different times in the same cases in proportion to the severity of the intestinal ulceration. They are more numerous in the severe acute cases and during the exacerbations of cases of moderate severity than while there is a continuous but moderate diarrhœa. In the early bloody mucoid stools they are numerous and evenly distributed. In the latter and less homogeneous evacuations they are plentiful, but less evenly distributed, being found chiefly in the grayish-yellow gelatinous masses, also but less abundantly in the particles of clear or rose-colored mucus; in the shreddy masses of detritus they are only occasionally found. In the homogeneous discharges of chronic cases they are less numerous than in acute cases, but are present in all portions of the stools. Even during intermissions of the diarrhœa, when the stools are soft or formed, they are to be seen in the particles of adherent mucus. In the progress toward recovery the amœbæ gradually disappear, but may be found after the stools have regained a normal appearance. Variations in size and activity are frequent: red blood corpuscles are found more frequently and in larger numbers in the more active amœbæ.

The reaction of the stool has a definite relation to the presence and activity of the organisms. In the alkaline and neutral stools they are active and numerous; in the acid stools they are scarce and only occasionally motile. The appearance of the amœbæ is well shown in the accompanying drawings. (Plates IV. and V.)

The fæces should be examined as soon after evacuation as possible, and at the body temperature, although this is not essential. In warm weather the organisms remain active for twenty-four hours after removal from the body; in cold weather warming the slide over an alcohol lamp will bring out active motion; for continuous observation a warm stage is to be preferred. Those portions of the stools which have been mentioned as containing the greatest number of amœbæ should be selected; but slight pressure should be made with the cover-glass; a magnifying power of about 400 diameters is sufficient. If not in motion, the organisms may be mistaken for degenerated cells or even starch granules, but with a little experience the larger ones can be recognized by their peculiar appearance and the gradual occurrence of the characteristic motion. In size the amœbæ vary greatly. Dock found the smallest 13 and the largest 37 mm. in diameter; the usual size is from 18 to 25 mm. In all of them the fine granular endosarc and the homogeneous ectosarc can be made out: the former is often filled with granules of variable size. In about one half a spherical highly refracting nucleus can be seen lying in a clear vesicle; also from one to numerous vacuoles. The inclusion of red blood corpuscles, leucocytes, bacteria, and detritus granules is common.

Additional Abdominal Symptoms.—Abdominal pain and tenderness, tenesmus, nausea, vomiting, and singultus occur with greater or less frequency in this form of dysentery. Of these symptoms colic is the most constant: it is observed oftener in the early stage of the gangrenous form, and in those of abrupt onset and during the acute exacerbations; as the diarrhœa subsides, so does the pain, which often disappears entirely as the gangrene progresses. In chronic cases severe colic is not prominent except during exacerbations, but a dull pain usually precedes and accompanies a movement of the bowels. More or less tenderness is excited upon pressure over the course of the colon.

Tenesmus, to which such great importance was attached by Woodward and Trousseau, was not present in a considerable proportion of cases as noted by Dutroulau and Councilman and Lafleur; in the writer's series it was generally observed, though not so marked as in catarrhal and diphtheritic forms. As reported by the last mentioned authors, tenesmus was specially apt to occur in grave cases with extensive sloughing. Irritability of the stomach attended by nausea and vomiting is most apt to be present at the onset, but is likely to occur at irregular intervals during the progress of the case.

Fever is not ordinarily a prominent feature in this form of dysentery, though if carefully observed a daily rise of temperature will be found to occur at some time during the twenty-four hours and extending through the course of the illness. Exceptions to this rule are the subnormal temperatures of gangrenous forms, the afebrile course of chronic cases, and the cases mentioned by Osler of the typhoid form, when fever may be high at times. Hepatic and pulmonary abscess always produces an elevated temperature. Under such circumstances the fever is of a continuous, remittent or intermittent type, ranging from 99° F. in the morning to 102° F. in the evening, and is likely to be accompanied by rigors and sweating.

Circulation and *respiration* are affected in proportion to the height of the fever. The pulse in cases of average severity ranges from 80 to 100; in chronic cases it is about normal, with progressive exhaustion; in fatal cases it becomes feeble and rapid, 120 to 140. The respirations are increased in frequency in proportion to the pulse rate.

The *urine* is generally slightly albuminous. In the gangrenous cases there is often retention and decided reduction in the quantity secreted.

4. SECONDARY DYSENTERY.

SYMPTOMS AND CLINICAL COURSE.—This form is likely to occur as a terminal event in various acute and chronic diseases. It is not infrequent in heart affections, Bright's disease, tuberculosis, measles, smallpox, and septicæmia. Woodward states that the association of diptheritic dysentery with the characteristic typhoid lesions of Peyer's patches was by no means of rare occurrence in the cases observed during the American Civil War. The occurrence of a complicating colitis may be manifested by the ordinary dysenteric symptoms, or the latter may be entirely absent, the intestinal affection not being suspected during life. In most instances there are only a few loose movements daily during the terminal stages of the primary disease. A. Brayton Ball mentions an illustrative case of dysentery following pyelitis, in which the patient had three or four loose movements daily for ten days before his death, without tormina and tenesmus, and with only occasional traces of mucus or blood. At the autopsy the colon was found riddled with ulcers, one of which had perforated the bowel near the sigmoid flexure. There was no peritonitis or lesion of the small intestine.

The important point to bear in mind as regards the symptomatology of secondary dysentery is that, contrary to the dictum of Woodward and Trousseau, extensive dysenteric lesions not only may exist in the absence of tenesmus and other symptoms, but that such latency is the rule in the secondary form. The absence of typical symptoms is sometimes due to the localization of the lesions in the upper part of the colon, but not always, as in some instances the entire large intestine is found to be affected.

COMPLICATIONS OF DYSENTERY.

Anæmia.—Reference has been previously made to the frequency and severity of anæmia as one of the symptoms of amœbic dysentery. It is here mentioned as a complication of all forms of the disease, in order to emphasize its importance and the necessity of combating it by proper measures of treatment. There is hardly any inflammatory disease characterized by such a rapid developing anæmia as occurs in dysentery. Niemeyer is authority for the statement that a general anæmic dropsy ensues more frequently after mild attacks of dysentery than after any other disease of equally short duration. Even in cases of moderate severity, ending in recovery in one or two weeks, the disturbance of nutrition is sufficient to protract the convalescence.

The chief factors explanatory of the blood changes of dysentery are as follows: (*a*) Impaired digestive power depending upon deranged and imperfect secretion of all the digestive fluids. Uffelmann, who has investigated the subject, finds the saliva is acid and contains a smaller number of salivary corpuscles than usual; the gastric juice is deficient in hydrochloric acid, and is proportionately weak in peptonizing power. The secretion of bile is diminished or temporarily arrested. Similar derangements doubtless occur with the pancreas and intestinal glands. (*b*) The continuous loss of blood and albumin in the stools; though the quantity passed each time may be small, yet frequent repetitions will effect the constitution of the circulating fluid. (*c*) The destructive influence of the amœbæ upon the blood corpuscles, these influences acting with greater or less severity according to the attack, but, as aforesaid, being prominent in all.

Peritonitis and Intestinal Perforation.—A localized peritonitis from the extension of inflammation to the serous coat in diptheritic dysentery, or occurring in the hepatic region in cases where that organ is involved, is of common occurrence. This process may become chronic and result in adhesions or may result in general peritonitis with a fatal issue. The condition, however, is most likely to ensue as a consequence of perforation of the colon resulting from sloughing of a deep ulcer, leading to a fecal extravasation and a rapidly fatal peritonitis. Perforation occurred in about 10 per cent. of cases collected by Woodward. It is most apt to occur in the cæcum, but may happen in any portion of the colon. In severe cases there may be an encapsulating process ending in pericæcal abscess, which may empty externally or into the bowel.

Intussusception is an accident only in very rare cases.

Hepatic and Hepato-pulmonary Abscess.—This complication occurs but rarely in the catarrhal or diphtheritic forms, but in amœbic dysentery, on account of the frequency and the additional gravity it lends the case, it becomes a matter of great interest and importance. Illustrative of the comparative frequency of liver abscess in the different forms of dysentery, the following facts are of interest: Woodward states that out of 156 cases of acute or chronic catarrhal dysentery without ulceration there was but 1 case of this complication, while in 115 cases of the diphtheritic form there were 3 of single abscess and 4 of multiple metastatic foci. In chronic intestinal ulceration (with which he includes the follicular and undetermined forms), out of 396 cases there were 6 instances of single large hepatic abscess, and 10 of multiple or metastatic, or about 4 per cent. Adding together these figures shows 14 cases of multiple abscesses and 9 of large single abscesses out of 511 cases in which the intestine was ulcerated, and but 1 case of large abscess in 156 cases of non-ulcerative dysentery. This experience corresponds with that of medical observers in Great Britain and Continental Europe, but differs very widely from that of British physicians in India and Burmah, of the French in Cochin China and Egypt, and of those who have studied tropical dysentery in Brazil, Chili, Venzuela, Mexico, and from recent statistics of amœbic dysentery as it has been observed in this country. Without going into details, it appears that abscess of the liver is found in one out of four or five fatal cases of tropical dysentery.

Showing the frequency of this complication in amœbic dysentery, out of 12 cases reported by Dock, 4 certainly, and probably 5, had liver abscess; 6 out of 15 in Councilman and Lafleur's series; and 1 out of 7 reported by the writer. Thus, out of 34 cases there were 12, or over one third, in which hepatic or hepato-pulmonary abscess was present. These figures correspond very closely with those of Ballingall, Annesley, Waring, Eyre, Ranking, Moore, Macpherson, Chuckurbutty in India, of Catteloup and Monret in Algiers, of Bougrael and Gayne in Cochin China, of De Castro in Egypt, as to the frequency of liver abscess in tropical dysentery, and would seem to confirm the identity of the latter with the amœbic form. Amœbic dysentery as observed in Europe appears to be an exception as to the enormous proportion of hepatic complications, and so far no reason can be assigned for this apparent exception. It is useless to mention the various theories which have been presented to account for the connection between dysentery and abscess of the liver, as the recognition of the identity of the specific causes of the intestinal and hepatic lesions has cleared the subject of much of its former obscurity. Speaking particularly of the amœbic or tropical forms, abscess of the liver may develop in any grade of severity or at any period of the illness. The gravity of the initial attack, instead of favoring, is prejudicial to the occurrence of this event, as patients are more likely to die from the severity of the intestinal lesions before infection of the liver has time to occur.

The period when hepatic involvement takes place varies between wide limits; it commonly develops from the fourth to the twelfth week. The most frequent site is the convex surface of the right lobe, the evidence going to show that in most cases infection takes place through the peritoneum, and that the right lung is involved by the passage of the organisms through the diaphragm.

I shall not discuss in detail the course and symptomatology of hepatic abscess, as that subject will receive attention in another part of this work, but will attempt to give only the salient points concerning the large solitary or tropical abscess.

The important symptoms are pain, irregular fever, and the development of a septic condition. Latent cases are not rare; these run their course without definite symptoms; sudden death occurs from rupture, and in a good many instances the abscess is discovered post-mortem, not having been suspected during life. The temperature is of an intermittent type; it may be normal or subnormal for a few days, and then rise to 103° or higher, being preceded by a rigor; the character of the febrile movement often causes it to be mistaken for malarial fever. The temperature may rise every afternoon without rigors. Profuse sweating is common. In chronic cases there may be little or no fever; this is especially apt to be the case where the abscess has opened. The pain is variable, and is usually located in the back or shoulder, or there may be tenderness and a dull pain in the right hypochondrium. The decubitus generally preferred is upon the right side. Physical evidences of enlargement are usually found; the latter may be so great as to cause bulging and projection two or three inches below the costal margin. Fluctuation and œdema of the chest wall may be occasionally detected. The appearance of the patient is suggestive: the skin has a sallow yellowish tint, the face is pale, the complexion muddy, and the conjunctivæ are infiltrated and bile-tinged. Marked jaundice is rare. Looseness of the bowels, and especially the detection of amœbæ in the stools, are very significant. Careful exploration with the aspirating needle will usually determine the diagnosis. In some instances the results are negative, even when exploration is made with a long, large-sized needle, in consequence of the viscidity of the abscess contents. Characteristic symptoms arise when the abscess invades the lung, which event is of not infrequent occurrence. Extension may take place through the diaphragm without rupture, producing a purulent pleurisy and involvement of the lung. In such cases the patients gradually develop a severe cough, usually of an aggravated, convulsive character.

The *physical signs* are those of consolidation at the base of the right lung, impaired resonance, feeble bronchial breathing, increased tactile fremitus, but the characteristic feature is the sputum: at first the expectoration is not peculiar, consisting of a little clear mucus, but it soon becomes more abundant, muco-purulent, and streaked with blood. After a short period, during a paroxysm of coughing the patient suddenly expectorates a large quantity of brick-red or brownish muco-pus, intermixed with more or less pure blood. Such expectoration is repeated daily with varying frequency throughout the illness. Budd and other authorities declare that this expectoration is pathognomonic of abscess of the liver perforating the lung.

Microscopical Characters.—The cellular elements observed are red blood corpuscles, leucocytes, round alveolar epithelial cells, oral epithelium, irregular fatty degenerated elements looking like liver cells. Elastic tissue fibres are frequently found in the later stages. Amœbæ are constantly present; they vary in number, size, and activity, and are found in all parts of the sputum, but are not so abundant as in the stools. The prognosis in these cases is serious, the mortality being over 50 per cent.; the death rate has, however, been reduced recently in consequence of improved surgical technique.

Pneumonia is not mentioned as a complication or sequel of dysentery by any of the systematic writers upon general medicine to which I have access, with the exception of Aitken, neither does Ball refer to it in his recent brochure upon the "Symptoms, Complications, and Treatment of Dysentery." This is rather a singular fact in view of the statements of Woodward, who says: "Bronchitis and pneumonia were common complications of acute dysentery during the war, particularly of the diphtheritic form. They were noticed especially after the occurrence of epidemic measles and after exposure to cold and inclement weather, particularly after marches during which the troops were insufficiently sheltered at night." Pneumonia occurred as an intercurrent complication during the advanced stages of the disease, usually in the croupous form, and was found in about one-fifth of all the autopsies of acute diphtheritic dysentery reported during the war. Very similar facts were observed with regard to the other forms of dysentery. In chronic ulcerative dysentery, not including cases complicated with tuberculosis, pneumonia was found (and often was the immediate cause of death) in more than one fifth of all the autopsies. It was observed in one fourth of the post-mortem examinations in which non-ulcerative inflammation of the intestine was found. The season of the year in which these pneumonic lesions were noticed is significant, a very large proportion occurring between the first of October and last of March. Aitken briefly mentions the frequency of pulmonic complications in the allied armies during the Crimean War. Griesinger alone, of all the writers on the diseases of hot climates, appears to have found pneumonia frequently associated with dysentery. In 96 autopsies of primary dysentery he found croupous pneumonia 7 times, catarrhal pneumonia 12 times, bronchitis with apoplectic foci 4 times, and gangrene 7, thus giving a proportion of nearly one third of serious pulmonary lesions and rivalling the proportion given by Woodward. It appears that pneumonia and other acute inflammatory diseases of the lungs do not occur with such frequency in tropical dysentery or in civil life as in camp dysentery, for the probable reason that exposure and the unhygienic conditions generally of armies in times of war render the victims of dysentery especially liable to pulmonary complications.

Pulmonary Tuberculosis.—Tubercular disease of the lungs is also a frequent associate of dysentery. Woodward found it to exist in nearly one sixth of all the autopsies of fatal cases of different forms of flux.

It was more common in chronic cases, but also occurred in the acute. In the first instance the tubercular trouble developed during the progress of dysentery, and in the acute form flux supervened in patients already laboring under phthisis.

Scurvy.—Reference has already been made to the influence of the scorbutic taint as a predisposing cause of dysentery. This association is developed where the diet is deficient in fresh vegetables and where it consists chiefly of salted meat. Sir Ronald Martin gives a terrible instance of suffering from this cause as it occurred in the European portion of the forces employed in Ava during the first Burmese War, where they were fed on salt rations for six and a half months: 48 per cent. perished within ten months, principally from dysentery complicated by scurvy. Such disasters have since been surpassed in the Crimean War during the winter of 1854–55 before Sebastopol, when the mortality was even greater for a similar combination of influences. The testimony of Woodward concerning the coexistence of scurvy with intestinal fluxes during the American Civil War corroborates the above experience. He says: "While openly pronounced scurvy was not very common, a recognizable but usually mild scorbutic taint was of more frequent occurrence, and whenever this made its appearance diarrhœa became prevalent, and showed an increased tendency to pass into dysentery and to become chronic." Elsewhere he expresses the opinion "that the scorbutic condition is not directly the cause of dysentery, but that no cachectic state is more favorable to the action of the other causes of these disorders or confers upon them a graver character when they have once been established." It is unnecessary to recapitulate any additional testimony upon this subject. Enough has been said to show that a combination of unhygienic conditions with insufficient and improper diet predisposes to both dysentery and scurvy, and will account for the frequent association of these diseases.

Malarial Fever.—Closely connected with scurvy as a complicating factor in intestinal fluxes is that of malarial fever. The connection between the two diseases is so intimate as to have given rise to the old but now obsolete idea that the infections of paludal fevers and of dysentery are identical. Aitken, in referring to the close association of these affections, illustrates it by citing the fact that "a boat's crew being sent ashore in a tropical climate, the probabilities are that of the men returning on board part will be seized with dysentery and part with intermittent fever." Such incidents do not prove a unity of causes, but only that the two etiological factors are coexistent, about which fact there is no dispute. An excellent opportunity for observing this connection was obtained during the American Civil War, when it was found that the great armies moving suddenly from the North to the malarial regions of the South were exposed simultaneously to the causes of dysentery and malaria, developing a hybrid disease, the symptoms resulting from each cause often appearing together in the same individual from the beginning of the case to its end. Sometimes, however, dysentery, either of itself or as a sequel to diarrhœa, appeared as the primary disorder, assuming subsequently a periodic form, either as to the flux itself or as to the accompanying fever; or ague or remittent fever made its appearance during convalescence from dysentery or after it had become chronic.

In other cases the periodic fevers were the primary morbid condition, and dysentery set in only after the health had been broken down by long continued ague or after remittent fever had been first developed. In still other cases malaria was manifested by chronic poisoning; the resulting cachexia, whether existing by itself or associated with mild scorbutic taint, was so widely spread as to favor the development of dysentery as well as diarrhœa. The subjects of this cachexia seemed less able to resist the causes of the disease than healthy men, and, once developed in them, dysentery, even in its simple or catarrhal form, was more apt to become chronic and to prove fatal. Not only were the ordinary forms of intermittent and remittent fevers observed, but occasionally paroxysms of pernicious malarial fever. Though the paroxysms were often obstinate and prone to recur, yet quinine was essential to control them, and its power in this regard was strong proof of the malarial nature of the complication. Notwithstanding the general consensus of opinion as furnished by army surgeons upon this subject, the diagnosis is beset with difficulties, and has doubtless often been made upon insufficient grounds.

Osler mentions the fact that with but one exception the cases of dysentery he has seen associated with intermittent pyrexia were due to suppuration. This observation is in accord with the writer's own experience in a hospital drawing its material from an extensive malarial country. I cannot recall a single instance of undoubted association of malarial fever with dysentery. It would thus appear that the malarial element is not so likely to be associated with dysentery in civil as in army practice. W. C. Maclean gives these symptoms of malarious dysentery: "Such cases will be recognized by the periodicity of the febrile paroxsyms, the presence of gastric irritability, such as we see in remittent fevers, and by the peculiar nature of the evacuations, which from the first are serous and contain but little blood, but have the characteristic dysenteric odor." Other writers mention the periodicity in the frequency of the stools, while the occurrence of chills is regarded as significant of malaria.

Such evidence is not conclusive, for fever of remittent or intermittent type, marked gastric symptoms, diarrhœal rather than dysenteric stools, and periodical exacerbations of the intestinal flux are symptoms recognized in dysentery when malaria can be excluded, while rigors with intermittent pyrexia and sweating are frequently indicative of suppurative processes in the liver or elsewhere. These facts should guard us against the hasty assumption of malarial infection, which can be diagnosticated with certainty by the discovery in the blood of the hæmatozoa malariæ.

Typhoid and Typhus Fever.—The combination of adynamic fevers with dysentery has been long recognized, and no doubt a tendency has existed to over-estimate their frequency by confounding the typhoid febrile symptoms which, as we have seen, are not infrequently developed in connection with certain forms of dysentery with true typhoid or typhus fever—an error which has been favored by the peculiar characters assumed by dysentery in certain epidemics. Many writers of the last century went so far as to describe dysentery as merely one of the varieties of typhus, giving it the name of "colotyphus," and looking upon it as the local manifestation of the typhus contagium; but since the anatomical test has been applied it was found that in many of the so-called cases of typhoid dysentery there was an entire absence of the characteristic lesions of typhoid fever, leading Rokitansky to express the belief that the coexistence of dysentery with typhoid fever is excessively rare. But that this complication does occur, and not infrequently, has since been shown by numerous observers—first by Trousseau and Parmentier in 1826; since by Parkes in India, by Baily at the Millbank Penitentiary, London, by Finger during an epidemic in the hospital at Prague, and by Lyons during the Crimean War. These observations were confirmed during the American Civil War, not merely by clinical observation, but by autopsy and preservation of the specimens in the Army Medical Museum. Woodward states it was so common to find the characteristic lesions of typhoid fever in the ileum and of dysentery in the colon that he was led to believe that the combination was likely to occur in every army where typhoid was the prevailing fever. The complication supervenes much in the same way as in malarial fever; that is, the continued fever and dysentery run their course simultaneously, or either appears as the primary disorder, to which the other was subsequently superadded. With reference to the coincidence of typhus fever and dysentery, aside from the brief statement that it does occur mentioned by several authorities, I find no details. My friend, Dr. C. Warfield, who has had an extensive experience with typhus fever in Northern Mexico, states that diarrhœa occurred in about 20 per cent. of the cases, and that occasionally dysenteric symptoms were present. The lesions of dysentery, however, were not confirmed by autopsies.

DYSENTERIC ARTHROPATHIES.

Since Sydenham mentioned the occurrence of joint symptoms in an epidemic of dysentery in 1672, they have been met with in numerous epidemics, as that of 1765, described by Lepecq de la Cloture and Zimmermann; 1776–77, described by Stoll; 1835, described by Thomas; and that of 1854 occurring in the canton of Montargis in France, described by Huette. In the American Civil War the pains in the limbs and back which were common in connection with both acute and chronic dysentery were in most instances, according to Woodward, rather due to malarial and scorbutic neuralgia than to rheumatism. Dewevre has recently made an interesting report upon this subject, giving the results of this complication in 65 cases, 15 of which occurred among 445 cases of dysentery under his care in the military hospital at Lyons, France, during the summer of 1885. He found the onset of articular symptoms to begin at variable periods of the dysenteric attack. Out of 60 observations in which the date of invasion was mentioned, in 9 it fell in the first week, in 7 in the second, and 44 in the first days of convalescence or several weeks later. Occasionally the development of the arthropathy is preceded by a sudden arrest of the intestinal symptoms, or the course of the joint lesion is interrupted by reappearance of the flux. In one case the alternation of articular and intestinal symptoms recurred three times in the same individual. The invasion is always sudden, and at first affects but a single joint. Of the 63 cases, the attack began in the knees 25 times, in the ankles 16 times, in the shoulders 9 times, in the elbow 4 times, in the hip once, in the right middle finger once, in the toe once, in the temporo-maxillary articulation once, and once in the sterno-clavicular articulation.

The SYMPTOMS are of slight intensity. There is but little pain, and either no fever or a slight and temporary rise of temperature, and no other disturbance of the general health. The patient usually first notices trouble with the joint upon making some slight movement. The ligamentous attachments are tender, with some swelling of the periarticular tissues; usually there is no effusion into the joint and no redness of the overlying skin. Hydrarthrosis may, however, occur, particularly in the knee, when it may distend the capsule and render movement difficult. Limitation to a single joint is exceptional, occurring in only about 8 per cent. of the cases. After a few hours or days other joints are implicated, but with less intensity, the last joint to recover being the one primarily attacked. All the joints may be attacked successively, but usually the number is limited to three or four. In cases of hydrarthrosis absorption is slow. Restoration of the functions of the joints involved, although sometimes requiring only a week, is usually protracted to a month or several months, and is most obstinate when the smaller joints are affected.

Neither ill health producing the dysentery nor a severe course of the disease seems to predispose to the arthropathies. On the contrary, they are more frequent in robust subjects, who have been but little weakened by the dysentery, than in the weak and cachectic, and in the mild rather than in the severe cases. Exposure to cold or over-exertion was not observed as a possible causal factor.

Various explanations have been offered to account for the connection between dysentery and arthritic troubles, but none of them are entirely satisfactory. Stoll and his followers, looking upon dysentery as a rheumatic affection, found a ready explanation in a simple metastasis to the joints. Others based the occurrence of arthropathies upon the existence of a " reflex relation " between the articular and intestinal lesions. Some of the observers regard the rheumatoid symptoms as the manifestation of a mild pyæmic infection. The most probable solution of the question appears to be that the joint affection bears the same relation to dysentery as it does to other infectious diseases—*e. g.* scarlet fever, typhoid fever, cerebro-spinal meningitis, dengue, etc.; that is to say, it is not a genuine rheumatism, from which it differs in many essential particulars, but it is the localization of the infectious agent or its products acting upon the joints through the circulation.

DYSENTERIC PARALYSES.

The most important contributions to the study of the paralytic complications of dysentery have been made during the latter half of the present century. Cases have been reported and the pathology discussed by various writers, notably Delioux de Savignac, Leyden, Barie, Weir Mitchell, Woodward, and Pugibet. The latter in 1888 gave a most valuable résumé of the subject, from which the details here given are mainly derived. Paralysis may occur in both the acute and chronic forms of dysentery, sometimes during the course of the attack, but usually as a sequel. By far the most common form is paraplegia. The upper extremities may be also involved; hemiplegic and monoplegic cases have been reported, and diffused general paralysis has also been observed. In some cases the onset is sudden, developing within twenty-four to forty-eight hours, and lasting but a short time—three to twenty-eight days. In other instances the paralysis has a gradual development, this appearing to be the usual history of the paraplegic form. Paralysis of the vesical and anal sphincters and girdle sensations are usually absent. The paralysis is rarely complete in all of the muscles of the limb or in muscular groups elsewhere. Among muscles innervated by the same plexus some may be affected and others not. Sensory disturbances are usually not prominent, but in some cases neuralgic pains, tingling sensations, cramps, and limited anæsthesia were observed. In an analysis of 17 cases reported by Pugibet, including his own and those of several other observers, in 13 the paralysis lasted four months, in 4 it was stationary at the time of the report, in 2 death resulted from the paralytic lesions, and in 4 it was independent of them. In speaking of the cases of palsy connected with dysentery, Weir Mitchell states that in nearly every instance there had been many possible causes, as long marches, bad diet, malaria, or spinal injuries, the latter being so common that almost any soldier long in the service had some to relate. It was thus difficult to fix upon any single factor as essential, as it was likely that several contributed to influence the result. The pathological condition underlying dysenteric palsies has not been satisfactorily studied, and the views which have been presented to explain their origin are largely theoretical: some of the reported cases were due to central lesions, and others were cases of multiple neuritis.

SEQUELÆ OF DYSENTERY.—Among the more important sequelæ especially of chronic dysentery are prolapsus ani, anal fistula from perineal abscess, and hemorrhoids, these conditions being largely the result of mechanical causes. Indigestion, irritability of the bowels, or obstinate constipation are not infrequent. Intestinal strictures resulting from cicatricial contraction after the healing of dysenteric ulceration, according to Woodward, are exceedingly rare. Profuse intestinal hemorrhage after subsidence of the dysenteric flux is a sequel mentioned by my colleague, Dr. Clopton, as occurring not infrequently in his experience. It is not, apparently, due to ulceration, but rather to a diseased condition of the walls of the intestinal bloodvessels and to the morbid state of the blood itself.

DIAGNOSIS OF DYSENTERY.—The recognition of the catarrhal form of dysentery is usually easy, the frequency of the stools, the presence in them of blood and mucus, the tormina and tenesmus producing a characteristic clinical picture. Local affections of the rectum, syphilitic and chancroidal ulceration, cancer, strictures, the presence of foreign bodies, and intussusception, especially in children, may produce straining and the passage of mucoid and bloody dejections. A careful physical examination in such cases will generally without difficulty determine the diagnosis. The *acute diphtheritic* form with its rapid and intense onset and severe constitutional symptoms may readily be mistaken for enteric fever. The higher temperature of dysentery, the aggravated intestinal symptoms, the presence in the stools in the early stages of blood and mucus, and later of diphtheritic sloughs, the absence of enlarged spleen, and the characteristic rose eruption of typhoid fever, should guide to a correct differentiation. The amœbic form can be recognized by a careful microscopic examination of the stools, which should be made in every case where, with a deterioration of the general health, anæmia, and impaired nutrition, there exists a disposition to looseness of the bowels. The irregular and chronic course of these cases should be borne in mind. A patient may not be bedridden, and even be in a fairly good condition, with well formed stools and very insignificant intestinal disturbance, and yet in the adherent particles of mucus in the fæces the amœbæ can be discovered. In such a patient an intense relapse is liable to occur at any time or a complication with liver or lung abscess. Cases are not rare in which the intestinal symptoms are either entirely in abeyance or so slight as to attract no attention until the occurrence of hepatic abscess, which may be detected during life by the presence of the symptoms heretofore detailed, or when rupture has taken place into a bronchus by finding the amœbæ in the sputum. In other instances the existence of amœbic dysentery and subsequent abscess of the liver is not recognized until revealed by the autopsy.

With regard to the diagnosis of secondary dysentery, attention has already been called to the fact that the absence of characteristic dysenteric symptoms is the rule in these cases, and that the intestinal complication is but rarely suspected during life. The knowledge that an extensive colitis, and perhaps ulceration, may be manifested only by a slight diarrhœa when it occurs during the terminal stages of some severe adynamic disease should not be lost sight of, as the prognosis in the presence of such a complication will be materially affected. The necessity of careful physical examination by touch and speculum in chronic cases, and where the rectum appears to be involved, has been previously mentioned.

PROGNOSIS OF DYSENTERY.—The prognosis in sporadic dysentery in adults is favorable both as to the certainty and speed of recovery, though it is to be borne in mind that a certain proportion may eventuate in the diphtheritic form, ultimately proving fatal, or others become chronic and pursue an indefinitely prolonged course. On the contrary, there is hardly any disease in which the mortality is more frightful than epidemic or diphtheritic dysentery. The circumstances upon which the epidemicity depends contribute very greatly to increase the mortality. It is unnecessary here to recapitulate these influences in detail: it suffices to say that impairment of constitutional vitality from long continued infraction of hygienic laws, over-exertion, loss of sleep, exposure, improper and badly cooked food, overcrowding, filthy surroundings, impure water, are the conditions associated with epidemics of this disease. When we take into consideration the further fact that it frequently attacks those whose powers are already enfeebled by the existence of some other severe disease, and when we consider the extent and severity of the intestinal lesions, we can understand that the death rate may vary from 50 to 80 per cent. The outcome of individual cases can be judged by the severity of the symptoms. Rapid emaciation and debility, dysenteric collapse, cool surface and extremities, dry, brown tongue, heart failure, anorexia and excessive thirst, tenderness of the abdomen, anxious countenance, shrunken features, sero-sanguinolent stools containing masses of necrotic tissue having a cadaveric odor, a putrid scent from the body, and persistent singultus, are symptoms of extensive intestinal sloughing and forebode a fatal ending. When diphtheritic dysentery supervenes during the progress of the chronic form, or occurs secondary to some severe acute or chronic disease, the patient, being already exhausted and emaciated, is apt to succumb in a few days. Less severe cases may assume a subacute type, often lasting a month and a half to two months, and may end in recovery or pass into a chronic flux of indefinite duration. It should not be forgotten that even extensive ulceration is not incompatible with cicatrization and cure.

The prognosis in children will be governed by the constitution and surroundings of the child, the ability of parents to execute proper measures of treatment, the season of the year when the attack begins, and the occurrence of complications. It goes without saying that the prognosis is more unfavorable when the child is already the victim of malnutrition from tuberculosis, rickets, or syphilis. The chances for recovery are worse in crowded centres of population, among the poor, in teeming tenement houses, where a change of air and proper alimentation cannot be secured. Cases beginning in the early summer are less hopeful than those occurring later. The prognosis is worse in children prematurely weaned and improperly fed or who have suffered with previous attacks of diarrhœa. Persistent fever, vomiting, rapid wasting, and severe nervous symptoms are of ill omen. "The form of stool which is of worst augury is that composed of greenish matter like chopped spinach in dirty brown, stinking fluid, and mixed with purulent mucus and blood;" the thicker and more homogeneous the motions become, although they may still be intensely offensive, the more favorable is the prognosis. Continuance of normal dentition, the appearance of tears, and, according to Eustace Smith, the occurrence of an eruption unconnected with the exanthemata, are signs of favorable import. Recovery is possible even in cases in which the symptoms are violent. Under no circumstances are the recuperative powers of nature in children more wonderfully exhibited than sometimes in aggravated cases of dysentery. I have seen restoration to health when high fever, vomiting, excessive purging, bloody and mucoid stools, rapid emaciation, and exhaustion would have seemed to render such a favorable ending hopeless.

The prognosis in amœbic forms, whether gangrenous, chronic, or of moderate severity, is always uncertain; the gravity of the disease lies in its tendency to persist: the latter is inherent, depending upon the nature of the lesions and the fact that they are so refractory to therapeutical measures. The frequency of hepatic complications, the constant tendency to chronicity in cases not rapidly proving fatal, are factors rendering it very difficult to foretell the result. A duration of two to four or six months in recovered cases and an average mortality of 33⅓ per cent. are about what can be expected.

TREATMENT OF DYSENTERY IN GENERAL.—*Prophylaxis.*—It is a truthful saying and worthy of universal acceptation with regard to dysentery, as of other infectious diseases, that "an ounce of prevention is worth a pound of cure." In the assumption of the infectiousness of this disease reference is especially made to the diphtheritic or epidemic and amœbic forms. The differences of opinion prevailing upon this subject are rather as to what constitutes infection or contagion than as to the real facts of the case, for, as stated by Woodward, "the majority of the great observers, no matter what their opinion in other respects, agree in regarding the dejecta as contagious."

Whether the evidence upon this subject is satisfactory or not, there can be no doubt as to the duty of the physician in the premises, both as a sanitarian and humanitarian, which is to take the safe ground, "to cry aloud and spare not" in teaching the doctrines of prevention, and in the execution of the same in his practice. These means consist, first, in the avoidance of all predisposing causes, or, in other words, in a strict obedience to well known hygienic laws. The selection of proper sites for camping grounds, barracks, and hospitals, the prevention of overcrowding in tenement houses, ships, and jails, the regulation of sewage, the care for the food and drink, the observance of the strictest cleanliness by authoritative control,—"all these" (as mentioned by Whittaker), "are general measures that suggest themselves in the prophylaxis of this or any disease." To which should be added the provision of proper clothing and shelter and the avoidance, as far as possible, of excessive fatigue and loss of rest. These rules, apparently simple, are not always easy of accomplishment. No doubt a great deal has been done in this direction in recent years, but the difficulties in the way of providing a proper quality and quantity of food and pure water supply are by no means easy to overcome; especially is this the case where large bodies of men are congregated, as in camps, armies in the field, prisons, tenement houses, also in the abodes of poverty, filth, vice, and ignorance, whether in cities or rural districts. Hence we find epidemic dysentery still occurring far too frequently. As to a proper food supply, without going into details it is sufficient to say that the constitutional state developed as a result of the continuous neglect of physiological laws in relation to nutrition, whether correctly called scurvy or not, is responsible for an enormous increase in the number and fatality of dysenteric disorders. But, however important a part has been and still is played by an improper regulation of the food, it fades into insignificance when compared with the evil of impure water. The writer does not wish to appear dogmatic upon this subject, but, having strong convictions, wishes to emphasize this point: That when the legend can be truthfully inscribed upon the doorposts of every house in the land, *Pure water only used here*, then will these desolating enemies of mankind, typhoid fever, cholera, and dysentery, cease to scourge, just as surely as the destroying angel passed over the bloodstained doors of the Israelites of old.

The problem to be solved is the prevention of fecal contamination of the drinking water. How difficult this is to accomplish is shown by the continued extensive prevalence of these diseases in spite of the knowledge which has been disseminated concerning them in recent years. While the information as regards the infective cause of dysentery is not so complete as in cholera and typhoid fever, yet we are fully warranted, nay impelled, to observe the same precautions with respect to the complete destruction of the infective organisms the stools may contain in dysentery. The word "destruction" is used advisedly in lieu of "disinfection," as the latter term is too often loosely applied and insufficient means employed to effect the purpose. The directions recommended by the American Public Health Association for disinfection in infectious diseases are in harmony with modern knowledge upon this subject. I shall not give these *in extenso*, as details can be found elsewhere. The most certain and potent disinfectant is fire. Every hospital should be provided with a furnace for the destruction of infected excreta; when heat is not available, the stools should be mixed with a strong solution of chloride of lime (four ounces to the gallon of water) or a solution of bichloride of mercury and permanganate of potash, two drachms of each to the gallon, the latter requiring a longer contact with the discharges, but having the advantage of being odorless. Careful attention should be paid also to the disinfection of the person and clothing of the patient. For the former purpose cleansing and sponging the body with a solution of appropriate strength of carbolic acid, chlorinated soda, chloride of lime, or corrosive sublimate will answer; the clothing and bed linen may be disinfected by immersion in a 3 to 4 per cent. solution of carbolic acid and thorough boiling.

Suspected water should be absolutely condemned. Every effort should be made to ensure pure water. The habit of drinking only that which has been previously boiled should be inculcated and encouraged by the physician in every way possible, not alone in the prevention of dysentery, but as a wise measure of defence against other infection. The practice of drinking water without previous purification from shallow wells, springs, ponds, tanks, marshes, and pools should be discouraged, as the water from such sources is specially liable to contamination from surface drainage. Running water, as in rivers and creeks, is more likely to purify itself, but should be protected from infection and cleansed by filtration and boiling. It is unnecessary to go into further details upon this subject, as the proposition will not be disputed that the enlightenment of an advancing civilization will under no circumstances be more beneficently displayed than in the perfection of the means of securing pure water. When the nations of the earth learn that to spend millions of dollars, if need be, for this purpose is the exercise of a true economy, then will epidemic dysentery and kindred diseases disappear.

MEDICINAL TREATMENT.—Before giving an outline of the management of the different forms of dysentery some general remarks upon the uses and powers of the principal medicinal agents advisable will be appropriate. At the outset it should be understood that there is no specific for any form of this disease.

As was demonstrated by Austin Flint the natural course of sporadic dysentery is toward spontaneous recovery in ten to fourteen days; so the effect of any remedy which apparently cures should be judged with this fact in mind. Specifics for the cure of dysentery have been vaunted from time immemorial. In 1736 the celebrated Pringle read a discourse before the Edinburgh Society for Improving Natural Knowledge, in which he claimed for a preparation known as Young's antidysenteric powder, or "*vitrium antimonii ceratum*," that it was a genuine specific for dysentery. The reputation of this medicine rapidly spread through Europe, but it was soon found to be uncertain in its action and often dangerous, so that after an extensive but brief popularity it fell into disuse. Such has been the fate of many other so-called specifics.

Ipecac is the remedy which has attained a greater reputation than any other as a specific for dysentery. Its use in this disease was made known by Piso in 1648; he described it as a "sacred anchor, as the most exquisite gift of nature," claiming that it not only evacuated the morbid humors by purging as well as by vomiting, but produced revulsion from the diseased intestine, and that an astringent effect succeeded its primary action. It was forgotten for a time until reintroduced by Adrian Helvetius as an antidysenteric nostrum. The secret was bought by Louis XIV. and given to the profession of the time, by whom it was regarded as a specific for dysenteric fluxes; but the belief gradually died out. Broussais used his influence against it, though it still continued to be prescribed by a few until in 1851 it was made the subject of a special essay by Savignac, who ascribed its beneficial results to not only its emetic and purgative action, but to its diaphoretic, sedative, and alterative influence. The article of Savignac did not attract much attention. In 1858, Docker, who had successfully employed ipecac on the island of Mauritius in the treatment of dysentery, called renewed attention to the subject. His plan of administration (the one still used) was, having put the patient to bed, to give a drachm of laudanum, apply a sinapism over the stomach, half an hour later to give from thirty to ninety grains of powdered ipecac, usually in a bolus; if this was vomited, he repeated the dose until it was retained. A single dose often sufficed for a cure, the pains promptly subsided, and the stools ceased. He gave it to patients of various constitutions and in all stages of the disease with equal benefit—out of 50 cases he lost but 1. The publication of Docker's results was followed by the rapid and successful introduction of his method in India, where it was advocated by Donaldson, Cunningham, Ewart, and others. In England it received the support of Waring, Maclean, and Aitken. During the American Civil War the ipecac treatment was not very thoroughly tested; its trial, however, at the Ecklington Hospital, Washington, D. C., and in an epidemic at Columbia, S. C., was not favorable. Better results have been reported at various times in medical journals of the United States by the non-emetic use of the drug in sporadic dysentery and also in chronic fluxes. It has been used to a certain extent on the continent of Europe, and, it is stated, with fair success during the late Franco-Prussian War. Maclean has been a most enthusiastic advocate of the ipecac treatment. He says in 1868, "a decade after the introduction of this treatment into India, that it is now almost invariably followed; it has reduced the former mortality by from 25 to 75 per cent.; it is, in his opinion, the most simple, the most successful, the most conservative treatment he has ever seen used in dysentery. Year by year under its use the number of chronic cases is becoming smaller and hepatic abscess less frequently seen." Joseph Ewart in 1883 speaks of it with the same enthusiasm. Numerous other writers in India corroborate these views. Recently, however, there has been a modification of opinion upon this subject. Dobie[1] says that the treatment by large doses of ipecac has fallen into disfavor. Chowdhovry says that both in civil hospitals and private practice it has been found unbearable in many cases. While neither of these writers have lost faith in the ipecac treatment, they advocate its use in much smaller doses. Upon this subject Woodward judiciously remarks: "It will be observed that in the most modern times the use of ipecacuanha in the treatment of the fluxes has re-established the reputation it enjoyed in the seventeenth century, and is regarded in many quarters with a confidence as blind as that reposed in it by Piso or Helvetius. Nevertheless, a little reflection must show the absurdity of expecting benefit from such a remedy in acute diphtheritic dysentery after the formation of the diphtheritic layer, in the chronic fluxes after extensive ulceration has already occurred, or in those cases which owe their virulence to the co-existence of a scorbutic or some other constitutional taint. It is easy to recognize, by the details of the majority of the successful cases recorded in which the virtues of ipecac are most lauded, that they were sporadic, for the most part mild acute forms, and against the small number of chronic cases reported to have been successfully treated must be offset the contrary results of the larger clinical experience of the Ecklington and Dreadnought hospitals." While the above is perfectly true, and while the ipecac treatment, in spite of oft-repeated trials, has never gained a foothold in this country, we must concede that in tropical and certain severe cases of catarrhal dysentery it is a remedy of great value: the number of those who testify upon this point and their reliability leaves us no room for doubt. It is possible, as suggested by Ball, that the discrepancy of results as obtained in America and India may be due to the fact that ipecac possesses especially curative powers in the amœbic form; if so, such results must follow only in the earliest stages, for it is only necessary to reflect upon the nature of the lesions to be convinced that we cannot rationally expect any immediate cure from ipecac or any other remedy after the intestinal ulceration has fairly commenced. As regards the use of this drug in much smaller doses, one to three grains every two to three hours, while this method has received the sanction of some of the highest authorities, the writer must express his skepticism, for the reason that, so far as he knows, there has been no systematic experimentation with this remedy alone: the exigencies are such that other remedies are generally prescribed at the same time, leaving the effects of the ipecac in doubt. Careful clinical observation only will settle these questions.

Opium.—The history of the use of this remedy in the treatment of intestinal fluxes is exceedingly interesting. Its unique and incomparable therapeutic powers have caused its administration to enter more or less into every plan of treatment of these diseases from prehistoric times down to the present day. It was of the effect of opium in dysentery that Sydenham wrote his celebrated eulogy beginning, "And here I cannot but break out in praise of the great God, the Giver of all good things, who hath granted to the human race, as a comfort in their afflictions, no medicine of the value of opium, either in regard to the number of diseases it can control or its efficacy in extirpating them."

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[1] *London Lancet*, 1888.

The position of opium as a remedy for dysenteric affections is a peculiar one. It has been used by those who abuse it, and abused by those who use it. The controversy as to its proper place and powers, which has been of very long standing, is still unsettled. Without attempting to enter fully into the history and merits of the disputation between the extremists on the one hand, who claim that opium is a sovereign remedy in all forms and stages of dysentery and has peculiar antiphlogistic powers, and those, on the contrary, who hold that it is productive of more harm than good, I shall endeavor to define its true place and powers in the treatment of dysenteric disorders. The fact that it has maintained its position for centuries in spite of the very strong opposition to its use and the excellent reasons for the same is very good evidence that opium is possessed of peculiar and positive virtues. As an analgesic it is unsurpassed. In a disease where pain, excessive intestinal peristalsis, loss of sleep, and ofttimes both primary and secondary nervous depression, play such an important part it is difficult to dispense with opium in some form or at some time, no agent having yet been found to equal it for the relief of these symptoms. The objection which has been strongly and truthfully urged against its use is that it produces anorexia, nausea, arrest of secretion, indigestion, nervous depression, constipation, and retention of acrid irritant contents of the intestine.

While freely admitting these evils, the practical conservative therapeutist still finds in opium a remedy difficult to dispense with. The ground taken by George B. Wood, Stillé, Flint, and a host of the followers of these great leaders of medical thought in this country, that opium exercises some special power in controlling the inflammatory process of the intestines, is not now regarded as tenable, for, as Ball pertinently asks, "What reason is there to suppose that in croupous and amœbic inflammations of the colon opium exercises any more of an antiphlogistic power than it does in typhoid infection of the small intestine or in diphtheria of the throat? For my own part," he says, "experience has taught me more and more to distrust the fallacious effects of opium in dysenteric diseases, and I am quite sure that this conclusion is in accord with most recent authorities." Accepting this warning, as well as that of Galen, who wrote, sixteen centuries ago, that "those who resort to anodyne remedies at improper times or immoderately jugulate the sick along with their pains," we still find an indispensable place for opium: especially is this true in severe cases of the catarrhal and diphtheritic forms, obviating its acknowledged evil effects by proper doses and judicious combination and alternation with other medicines. Not expecting any specific effect upon the inflammatory or ulcerative process, we give it to ease the pain, to reduce the excessive frequency of the actions, to control morbid peristalsis, to relieve the agonizing tenesmus, to afford needed rest, and to overcome the profound nervous shock incidental to the diseases we are dealing with. It is for these reasons that those who have urged the strongest objections against the prescription of opium have themselves employed it while abusing it, and, having most excellent grounds for so doing, they are nevertheless compelled to use it. Until some remedy is found which possesses the therapeutical powers of opium without its objectionable features it will still occupy a prominent place in the list of remedies for the treatment of dysenteric diseases.

Purgatives.—Mild purgation for the purpose of evacuating the alimentary canal of the peccant humors, being in accordance with the humoral pathology, has been resorted to in the treatment of intestinal fluxes from the earliest times. It was generally admitted that drastic cathartics were objectionable, on account of their irritant effects; hence the milder laxatives, especially those having an after astringent effect, were preferred. According to modern views, purgatives are used in the treatment of dysentery to fulfil the following indications: (*a*) To cleanse the alimentary canal of various irritants, as undigested food, hardened fecal masses, and decomposing secretions; (*b*) to increase and modify intestinal and other glandular secretion, thus aiding absorption and assimilation; (*c*) by increased secretion to favorably influence congestive and inflammatory processes of the intestines. The remedies which have been most extensively used to accomplish these ends are *rhubarb, castor oil, calomel*, and the *salines;* of the latter especially the sulphates of soda and magnesia. As to *rhubarb*, while its secondary effect may render its use occasionally advisable in mild cases or in children with irritant intestinal accumulations, its tardy, uncertain, and painful action renders it generally objectionable.

Castor oil, on account of its certain, rapid, and generally unirritant action, has been extensively used, especially in England and the United States. Illustrative of the extent of its consumption, Woodward states that nearly a quarter of a million of quarts were purchased by the purveying department of the army during the four years of the American Civil War, and either alone or combined with laudanum or turpentine it was the favorite purgative in dysentery. It is not now very often prescribed for adults on account of its nauseous taste, and the fact that it is a simple evacuant; it is, however, quite frequently given with advantage in the mild fluxes of children, as well as of adults, in the form of emulsion and in combination with opiates to obviate any griping effects.

Calomel appears to have been first used in the treatment of dysentery early in the seventeenth century. It was very extensively employed, and an immense amount of harm done with it during the first half of the present century. It was used not only for its effects upon the intestinal canal, but in conjunction with mercurial inunctions and opium in order to produce salivation. The extent to which it was misused is almost incomprehensible. Cunningham in 1805 gave it in twenty-grain doses repeated two or three times a day, one of his patients taking in this way three hundred and sixty grains. In ordinary dysenteries Johnson was content to give daily twenty-four to forty-eight grains of calomel with two to four grains of opium and ten to fifteen of antimonial powder or ipecac. The enormous mortality necessarily resulting from such heroic medication did not appear to disabuse the minds of those who resorted to it: it was not until 1844 that this practice ceased in India, but calomel continued to be used in more moderate doses until 1860, when it was displaced almost entirely by the ipecac treatment. The abuse of this medicine in Europe and in the United States was notable, but not so great as in the tropics.

During the American Civil War calomel was extensively used in the treatment of dysentery. It was misused to such an extent, in the opinion of the Surgeon General, that he issued an order directing that it be struck from the supply table of the army, and that no further requisition for this medicine should be approved by Medical Directors. While this piece of official despotism was denounced by the American Medical Association as "an unjust charge of wholesale malpractice against the army surgeons, and as unwise and unnecessary," it illustrates the change of opinion upon this subject, for, though it was so extensively used twenty years ago, Ball comments upon the fact that Osler does not even mention calomel as a remedy for dysentery in his recent work upon the Practice of Medicine.

In spite of the terrible abuse of this remedy in the past, and the fact that it has been negatively placed upon the black list by such a high authority as Osler, the writer is of the opinion that calomel judiciously and carefully used fulfils some important indications in the treatment of dysentery: especially is this the case in the presence of malarial complications. Here and in similar conditions, where there is a morbid condition in the processes of absorption and secretion of the alimentary glandular organs, calomel exerts a unique beneficial influence. It should not be used as a purgative, for we have those which are milder and more rapid, but solely for its alterative effect, which can be obtained by small doses and without harmful results.

Saline Purgatives.—The salines have long sustained a well deserved reputation in the treatment of dysentery. In many respects they are superior to any other purgative. As cleansing agents their rapid action, the increased secretion produced by them, their mildness and certainty, are special advantages; in addition to which they are acceptable to the stomach, deplete the intestinal bloodvessels, and, it is claimed by some, increase the secretion of bile. Rapidly following their use the bloody and mucous stools are replaced by free liquid fecal dejections; the tormina and tenesmus are relieved; many cases of the sporadic form require no other treatment than a free saline purge. The sulphate of magnesia or sulphate of soda are to be preferred. Details as to methods of administration and dosage will be hereafter mentioned.

Vegetable and Mineral Astringents.—Remedies of this class administered by the stomach have been more or less extensively used in the treatment of intestinal fluxes for centuries. It will only be necessary to speak of a few of them as representative of the class. They are advised for the supposed effect of checking excessive and abnormal secretion and of stimulating to healthy action an inflamed or ulcerated mucous membrane.

Tannic or *gallic acid* will doubtless represent all the virtues of the vegetable astringents; of the minerals, the salts of iron, lead, copper, and silver are typical. Most of the members of this group have very properly been discarded in the treatment of dysentery. Nitrate of silver, however, still has the sanction of high authority, especially in chronic cases. In its administration the question always arises, How can we rationally expect a half grain of this easily altered salt to run the gauntlet of chemical change from stomach to colon, and then produce any material effect upon the extensive surface of the latter, as it is generally given in combination with other remedies? The verdict upon its use by most clinicians will be "utility doubtful."

Antiseptics.—The most important agents of this class are bichloride of mercury, the salts of bismuth, creasote, carbolic acid, salol, naphthalin, resorcin, creolin, tricresol, etc. These remedies have been advised for use *per os* upon the germicidal theory, and prescribed with varied success in dysentery and kindred affections. Without stopping to discuss the merits of this theory, or how far it is practicable to reach from above and destroy infectious organisms in the colon, let us view them from a clinical standpoint.

Corrosive sublimate was recommended by Kopp in 1827, subsequently by Eisenmann and Parkes, more recently by Ringer; the latter claims that in the acute fluxes with frequent bloody, slimy stools rapid relief is effected by hourly doses of $\frac{1}{100}$ to $\frac{1}{120}$ grain. It perhaps may do good in some cases, but its virtues have not been generally substantiated.

Subnitrate, Subcarbonate, Subgallate, and Salicylate of Bismuth.—These salts of bismuth produce very similar results, and the consensus of opinion is decidedly favorable as to their beneficial action, more especially in the chronic fluxes. Exactly the *modus operandi* of bismuth is not known positively: judging by its local effects, we conclude that it is slightly astringent, antiseptic, and protective. When perfectly pure it can be given in such large doses (thirty to sixty grains) as to ensure its passage through the colon. It subserves its best purpose after the acute stage has passed and the intestine has been emptied of all irritant contents. In chronic cases it aids in the healing process and decreases the frequency of the stools.

Creasote and Carbolic Acid.—The well known antiseptic and antiputrescent power of these drugs commend them for trial in dysentery. The difficulty to overcome in their use is to introduce them in sufficiently large quantities to produce an antiseptic effect upon the intestine without poisoning the patient. So far, this objection as to carbolic acid has proven to be insuperable. Recently creasote has been given in much larger doses in the treatment of tuberculosis than was formerly thought possible; though it has been warmly praised in some quarters, its positive value in dysentery has not been established.

Naphthalin, resorcin, salol, and numerous other members of the phenol group have been advised and, especially the latter, extensively used in dysentery and kindred affections upon the ground that effectual intestinal antisepsis could be produced by them without danger of toxic effects. Good results have been claimed for naphthalin given in five-grain doses three or four times daily. I can speak of the value of salol from quite an extensive experience in the acute diarrhœas and dysenteries of both children and adults, as well as in the obstinate looseness of the bowels in the amœbic form. Combined with large doses of bismuth, it appears to exercise better control over this obstinate diarrhœa than any other remedy. It can be given in large doses (twenty grains to an adult) and kept up for days without harmful results.

Tricresol.—A combination of ortho-, para-, and metacresols, constituting tricresol, now obtained in a pure state from coal tar, has recently been the subject of studious investigation by chemists, bacteriologists, and surgeons in Germany and elsewhere. This new claimant for antiseptic honors is said to possess decided advantages over its older competitors—viz. that it will act in the presence of albumin, and that, being five times as powerful as carbolic acid, it will produce intestinal antisepsis without danger. H. Kolch reports 12 cases of typhoid fever recently treated with this agent alone, giving it in doses of one and one half grains dissolved in olive oil by means of potash soap in capsule three times daily after milk. The result was rapid convalescence in thirteen to eighteen days and an absence of all severe symptoms. If these favorable reports are confirmed, the remedy commends itself in the treatment of dysentery, both by the stomach and by injection of a solution in the bowel.

Medication by the Rectum.—The plan of treating inflammatory diseases of the lower bowel by direct medication through the rectum is not new: on account, however, of various difficulties it did not grow into general favor until in recent years. The objections to rectal medication which have been urged are the pain incident to the introduction of the tubes in the anus, the irritability of the rectum causing expulsion of the injection, and the uncertainty of the amount of the drug absorbed. The advantages, however, of local treatment are so positive as to warrant the efforts which have been made to overcome the objections, and probably the greatest advance made in the treatment of dysenteric diseases has been in the extensive use of local means. The indications fulfilled by rectal treatment are (*a*) by thorough irrigation with simple warm or cold water to cleanse the rectum of all irritant contents; (*b*) by astringent and alterative remedies to stimulate healthy action of the inflamed or ulcerated mucous membrane and control excessive serous exudation; (*c*) by the use of antiseptics to destroy infective organisms; (*d*) by the local action of anodynes to produce a more rapid and powerful effect than when the remedy is introduced by the stomach. Rectal tenesmus and premature expulsion of the enemata can best be overcome by the previous injection of a cocaine solution or by throwing into the bowel half a drachm of laudanum in half an ounce of warm starch-water. To thoroughly irrigate the colon one and a half to two quarts are necessary. A large sized Nélaton's catheter or a rubber tube made for the purpose, having been gently introduced eight or ten inches, should be connected with a fountain syringe or funnel, with the patient in the knee-elbow position or with the hips elevated on a pillow. The injection should be allowed to flow very gradually into the bowel, the connecting tube being compressed occasionally and the abdominal wall gently kneaded in the direction of the colon from below upward, to allow the intestine to adapt itself to the distending process and prevent a possible rupture. Very happy results have followed simple irrigation with boiled water, the griping pains and frequency of the stools being rapidly reduced. In other cases a solution of common salt or borax, about two drachms to the pint of water, has a better effect. The use of medicated injections will be mentioned in connection with the special treatment.

TREATMENT OF CATARRHAL DYSENTERY.—Confinement to bed is necessary in all cases; the attempt to be up and to take exercise of any kind is prejudicial. The diet should be carefully regulated; no solid food should be taken; milk, chicken, and meat broths, and light farinaceous articles, should constitute the nourishment. The bowels should be cleared out by a saline, half an ounce of Epsom, Glauber's, or Rochelle salt; if one dose should not act freely, it may be repeated; the occurrence of free watery stools is usually followed by a relief of the symptoms. If there is a disposition to excessive peristalsis, the salts can be followed by an opiate with bismuth or salol combined with the latter, as in the following prescription:

℞. Bismuthi subnitratis, ʒiij;
Salol, ʒj;
Pulveris opii, gr. vj.
Misce et in chartulas No. vj dividenda.

Sig. Take one powder every three or four hours according to frequency of the stools.

In two or three days it may be necessary to repeat the saline. Or the case can be treated from the beginning by giving small doses of salts, one to two drachms, in combination with four to five drops of tincture of opium, taken three or four times daily. The milder cases may be relieved by simply washing out the colon with three to four pints of warm water.

TREATMENT OF DIPHTHERITIC DYSENTERY.—The problem of treatment here is not so simple. The lesions are so severe that many cases will die in spite of everything that can be done. The indications are to (*a*) sustain the patient's powers by nutritious, unirritating food, and by the free use of stimulants, alcohol and strychnine; (*b*) to counteract malarial complications by the use of quinine, and scurvy by fresh vegetable diet; (*c*) to relieve pains, obviate nervous depression, produce sleep, and hold in check the excessive frequency of the stools, for which purpose opium in some form is demanded; (*d*) to cleanse the intestine by the occasional and moderate use of salines; (*e*) to produce a healing, protective, and antiseptic effect upon the bowels by the use of such remedies internally as bismuth, salol, creasote, turpentine, tricresol, naphthalin; (*f*) to cleanse the bowel by irrigation and to medicate it by injections of antiseptic and astringent remedies.

In a disease characterized by such profound constitutional depression the careful selection and administration of food become a matter of great moment. The digestive powers are impaired; hence peptonized milk, milk with lime or Vichy water, koumyss, or matzoon, liquid peptonoids, chicken broth, beef juice, should be prescribed—in other words, concentrated nutritious food that will be largely absorbed and leave no irritant débris. Alcoholic stimulants in the form of good whiskey, brandy, and champagne are necessary as soon as adynamic symptoms are noticed, or even to anticipate them when we are sure of the diagnosis. Strychnine is useful, not only for its stimulant effect upon the heart, but for its tonic effect upon the muscular coat of the intestine. Quinine is required whenever a malarial factor is present: it should be given in antiperiodic doses, fifteen to thirty grains daily, until the malarial element is eliminated. Small doses of calomel may also be required in the presence of this complication. If a scorbutic taint is suspected, lemon or lime juice, onions, watercresses, and other fresh unirritant vegetables are required and produce rapid improvement.

It is difficult to dispense with opium in this form of dysentery; it may be given by injection into the bowel, thirty or forty drops of the tincture with half an ounce of warm starch water, repeated often enough to control the excessive frequency of the stools, the violent tenesmus, and counteract the nervous depression. Its tendency to cause retention of the irritant intestinal contents may be obviated by an occasional saline or irrigation with hot water. If the rectum is too irritable to retain an enema of laudanum, morphine may be given hypodermically, or powdered opium by the stomach, the latter in doses of one to two grains every three or four or six hours, according to effects. A combination of opium with large doses of bismuth and salol or creasote is an excellent one in severe cases, as in the following prescription:

℞. Bismuthi subnitratis,	ʒvj;
Tincturæ opii deodoratæ,	ʒiij;
Creasoti,	gtt. xxiv;
Aquæ menthæ piperitæ,	℥vj.—M.

Sig. Take one tablespoonful every three or four hours.

Cocaine given internally often has a happy effect in obviating tenesmus; it may be given in doses of one to two grains every four or six hours. Cleansing enemata can be followed by antiseptic injections, as of creolin or tricresol, ʒij–ʒiv, in a quart of warm water. Injections of carbolic acid or corrosive sublimate are dangerous, because if used in sufficient quantities to avail as germicides they are apt to produce toxic effects. Ordinary astringent injections, as of alum, tannic acid, acetate of lead, or nitrate of silver, may be of service when the stools are large and serous.

TREATMENT OF AMŒBIC DYSENTERY.—In the early stages, before the ulcerative processes have fairly commenced, the ipecac treatment finds its application. It is possible that the remedy may have some destructive effect upon the organisms; at any rate, the testimony, as previously related by those who have tried it in tropical dysentery, is conclusive as to its value. It is necessary to take precautions that the ipecac should be retained: the nauseant or emetic effects are not desired; the stomach should be quieted by the previous administration of thirty drops of laudanum or by hypodermic injection of one quarter grain of morphine. It should be empty: no liquid should be allowed. A large mustard plaster is applied to the epigastrium, and half an hour after the opiate thirty grains of ipecac given in a bolus; the dose may be repeated the second or third time, or it may be given in smaller quantities, five to ten grains in repeated doses.

The diet in this form of the disease is a matter of great importance. Upon this point Ball quotes from Graves's *Clinical Lectures*, in which he says: "I have found several cases which had obstinately resisted the most varied remedies assiduously employed get well rapidly after a liberal allowance of meat was given; and at present, when called on to treat a case of dysentery of long standing, the first thing I do is to put my patient on full meat diet." I can add my testimony as to the value of this suggestion. The ordinary dietetic rules are not applicable in amœbic dysentery or in any chronic form. There is hardly any disease characterized by such rapid anæmia and wasting: it is nothing unusual to find patients taking the ordinary diet of milk and slops to lose in weight a pound daily, or to find them gain rapidly when placed on a full diet of nitrogenous food, as scraped meat, raw or slightly cooked, soft-boiled eggs, broiled fish, nutritious soups, or cooked tender meats when the patient will chew them thoroughly. A moderate amount of toasted bread can be allowed under the same restrictions. Rectal injections of a solution of quinine from 1 : 5000 to 1 : 1000 have been recommended by Osler, Councilman and Lafleur, and others, from a suggestion by Lösch, who found that the amœbæ were killed by such solutions outside of the body. The beneficial result of this treatment is *sub judice*. My personal experience was not satisfactory; the matter will have to be determined by further trial. There can be no question, however, as to the value of nitrate of silver injections: the bowel having been first washed out by a large enema of warm water (two quarts), introduced gently and slowly, as previously suggested, is to be followed by the silver injection, 30 grains to the quart. This should be retained as long as possible and given twice daily. Strong injections of small quantities do no good, as they fail to reach the ulcerated surfaces. Other astringents are useful, as sulphate of copper, alum, and acetate of lead, but generally are inferior to the silver salt. Injections of corrosive sublimate have been recommended by some high authorities. I have already mentioned the objections to this agent: if used in small quantities, it will not reach the extensive surface of the colon; if in large quantities, it is likely to be absorbed and produce serious poisonous effects. The same objection applies to carbolic acid. Next to nitrate of silver, I have found creolin to produce the best results; it can be used in the proportion of half an ounce to the quart of warm water. Iodoform is inapplicable, on account of its insolubility and the large quantity required. Tricresol is an antiseptic which is likely to prove of value.

Opiates are not usually indicated in this form of dysentery, except perhaps in the gangrenous form to restrain excessive peristalsis and give the patient rest. Large doses of bismuth (thirty to forty grains) and salol in ten- to twenty-grain doses are of distinct value for the arrest of obstinate diarrhœa. The above suggestions are also applicable to non-amœbic forms of chronic dysentery. A change of climate or a sea voyage will sometimes effect a cure when other means fail. The mineral acids, preparations of pepsin, iron, quinine, arsenic, and strychnine are of service in promoting nutrition and as aids to counteract anæmia.

Reference has been made to the necessity of requiring patients with dysentery to assume the recumbent position. This is a matter of such importance in all forms of the disease that reiterated attention is called to it. Except in very chronic cases, where the intestinal symptoms are to a great extent in abeyance, and where gentle exercise may be permitted, the patients should persistently remain in bed; they should not be allowed to get up for any purpose: the sitting posture which many patients insist upon while at stool favors very decidedly both the pain and the frequency of the dejections. They should also be taught to restrain as much as possible the desire to empty the bowel.

Some remarkable cures have recently been reported of chronic dysentery by the use of an infusion or fluid extract of a plant growing in Mexico and Southwestern Texas known as the *chapparro amargoso.* R. T. Knox of Gonzales, Texas, reports the cure of a long-continued and most obstinate attack of chronic (probably amœbic) dysentery, of which he was himself the victim, by the use of this remedy when all other means faithfully tried had failed. Similar good results have been recorded by J. W. Nixon and others. The remedy is not narcotic, but excessively bitter and astringent. In doses of one half to two drachms of the fluid extract it produces no disagreeable effects. The reported cases are too few to predicate any basis for a positive opinion as to the virtues of this drug, but chronic dysentery is a disease so difficult to manage that any agent offering a prospect of doing good is worthy of trial. The fluid extract can be used in the doses mentioned, and can be prescribed in connection with the other treatment suggested.

The management of non-amœbic forms of chronic dysentery is practically the same as herein given.

I have now under observation in my wards four cases of dysentery, ranging in duration from six weeks to six years. A trial is being made with chapparro in very much larger doses than as above mentioned, one of these patients taking an ounce of the fluid extract every four hours, the average dose being half an ounce every four to six hours. In two cases various other methods of treatment had been used without any decided benefit. In order more thoroughly to test the virtues of the remedy, every other medicine was discontinued, and only the ordinary precautions as to diet and quietude are enforced. While I am not able to pronounce absolutely as to the final result, the symptoms have been rapidly ameliorated: one case is apparently cured, the others decidedly improved. The effects were more pronounced from the fact that when the supply of the drug was exhausted the patients relapsed, and again improved when the medicine was resumed.

The compound tincture of benzoin, in doses of half a drachm, repeated every three or four hours, is an excellent remedy for the relief of intestinal hemorrhage, previously mentioned as an occasional complication.

THE PLAGUE.

BY WILLIAM M. WELCH, M. D.

SYNONYMS.—English: The Bubo Plague, The Pest; Latin: Pestis, Pestilentia, Pestis Inguinaria; French: La Peste; German: Die Pest, Beulenpest.

DEFINITION.—The plague is an infectious febrile disease which has prevailed epidemically at different times in various countries, and is characterized by buboes or swelling of the inguinal or other lymphatic glands. It is frequently attended by carbuncles, petechiæ, or purpuric spots distributed over different parts of the body.

HISTORY.—During the Middle Ages, and even at a later period, almost every variety of pestilential disease that prevailed in epidemic form and was attended by great mortality was included under the term "plague." It is believed that Galen was largely responsible for this confusion by reason of a definition given by him, as follows: "When a disease attacks a number of persons in one place, it is an epidemic; and when many are destroyed, it is a plague." But a gradually increasing knowledge of diseases has resulted in a differentiation so distinct and definite that confusion of terms no longer exists: those terms which formerly applied to a large group of diseases have either been limited to certain maladies or discarded altogether, while new names have been found for the others. The term "plague" is now restricted, as the definition indicates, to a contagious febrile disease presenting certain definite symptoms and pathological processes, most prominent among which are the formation of buboes.

No very reliable account of the plague is to be found previous to the sixth century, although it is believed to have existed in Egypt, Libya, and Syria before the Christian era. The first extensive epidemic of the disease in Europe occurred in Constantinople in the year 542 A. D., during the reign of Justinian, and hence has frequently been spoken of as the Justinian plague. From that time until the latter part of the seventeenth century plague epidemics frequently occurred in Europe: so frequently, indeed, that this disease was more dreaded than any other that prevailed. It was especially rife and fatal during the Middle Ages, and even continued in various countries as a devastating scourge for a few centuries later.

In the seventeenth century there were, according to Sir Gilbert Blane, no less than forty-five epidemics of the plague in various parts of Europe. Fourteen of these occurred in Holland, where the disease was introduced by the Dutch engaged in the Levant trade. From Holland the infection was conveyed to England, and in that country as many as twelve epidemics occurred. The most notable epidemics in both of these countries were in 1665. This has often been termed the year of the "Great Plague." The disease spread with such great rapidity and manifested so much virulence that, it is said, 7165 deaths occurred in a single week, and no less than 68,526 in one year, in the city of London and its suburbs. When we consider the population of London at that time, it is evident that this was a very large mortality rate.

After a long interval of comparative absence of the plague, it reappeared in the early part of the eighteenth century. It was met with most frequently in the Turkish dominions. During this century no less than nineteen epidemics occurred in Egypt and nine in Turkey. Epidemics occurred also in Germany, Russia, Spain, Poland, Greece, Italy, Sweden, and France. An epidemic most notable for its severity visited Marseilles in 1720–21. Within the present century the disease has prevailed at different times in Egypt, Turkey, Greece, and Russia. It has also visited Germany, Syria, Italy, Persia, and some other countries. In 1844 the disease disappeared from Europe and Asia, but reappeared with great virulence in Arabia in 1853, and somewhat later was seen in North Africa, Persia, and Hindostan. During the period from 1873 to 1877 the pestilence prevailed with unusual severity in almost every part of Arabia. In 1878–79 it committed great ravages in Astrakhan. The most recent epidemic of the plague occurred in China in 1894. It prevailed in Hong-Kong, Canton, and some other districts. Owing to the ignorance and superstition of the Chinese, no reliable statistics could be collected, but it is known that the epidemic was very severe and fatal. Fortunately, this pestilential disease has never visited America, or, if it has been seen at all, it has never prevailed in epidemic form.

ETIOLOGY.—All modern authors concur in the belief that the plague owes its origin to a specific contagium. While the disease has always been confined to the Eastern Hemisphere, yet it is universally admitted that the contagium is not indigenous to any country or soil. There is no doubt, however, that certain circumstances may combine to favor the propagation and action of the infecting principle—such, for example, as poverty, overcrowding, personal uncleanliness, improper or insufficient food, and the like. All observers agree that the physical and social wretchedness resulting from poverty is, except the contagium itself, the most potent factor in the spread of the disease. While this fact has been noticed in all epidemics, it was so conspicuous in the great epidemic of London in 1665 that the writers who described the disease at that time termed it "the plague of the poor."

Certain local conditions are also known to be favorable to the spread of the plague. In the Eastern countries, where the disease prevailed in past ages with such great virulence, the state of civilization was wretchedly low, and a large proportion of the inhabitants were not only insufficiently fed or forced to subsist on the most unwholesome food, but lived in crowded dwellings that were poorly constructed and badly ventilated. No regard whatever was paid to sanitary laws. Improper drainage existed in all cities, towns, and villages; masses of decomposing animal and vegetable matter, including human dejecta, were allowed to accumulate; human corpses were commonly kept too long before burial, and even then they were interred at an insufficient depth; the dwelling-houses had simply an earth floor, and not infrequently a horrible odor was emitted from the decomposing dead bodies of some previous occupants who had been buried only a few feet beneath. When such a deplorable condition exists, it is not surprising that the plague, once introduced, should linger and commit great ravages. After the introduction of better sanitary regulations in Egypt and Turkey, in 1844 the plague disappeared, but it returned again ten years later, when these regulations were disregarded. The importance of sanitary measures was fully realized in China during the recent epidemic. A committee of the Sanitary Board has emphatically expressed the opinion that the speedy stamping out of the plague in that country in 1894 was due to thorough cleansing and disinfection of the houses in which cases had existed.

Whatever the local conditions or the habits of the people of any country may be, the plague never originates autochthonously, as was formerly supposed, but is always introduced by a previous case and communicated from one person to another. The theory that the disease is spread by infection has, it is true, often been assailed, and evidence to prove its non-contagious nature presented, but all modern authors agree that the preponderance of testimony is to be found on the affirmative side of the question. Even the Turks, who are not very familiar with the theories taught in more enlightened countries, have gradually arrived at the conclusion that the plague is infectious. It would appear, however, that in order for an epidemic to arise and continue with great severity certain favorable local conditions must be present—such, for example, as have already been described. So also moderately warm weather and dampness or a marshy conformation of soil, such as exists at the mouths of rivers, are favorable to the development and spread of the disease.

Individual predisposition to the plague varies, as in most other contagious diseases. Some persons appear to be entirely immune, while others take the disease after the slightest exposure. Sex exerts no influence whatever over the predisposition. Intemperance and all habits that depress the vital forces, if they do not render the individual more susceptible, are sure to predispose him, if attacked, to a severe form of the disease. Age appears to exert some influence over the predisposition, as it has been observed that persons over fifty years of age are seldom attacked. The plague differs from most other infectious diseases in that one attack does not confer immunity against subsequent attacks.

Although bacteriology has not brought to light any specific microorganism to explain the infectious nature of the plague, yet such a pathogenic germ is believed to exist. That the disease is really infectious has been demonstrated in various ways. Many instances are recorded of the contagium having been conveyed from one city or locality to another by means of infected individuals. On the other hand, it has never been known to originate in any district or island which has had no communication with an infected locality, but, like infectious diseases in general, it follows the line of travel. The disease has often been confined to an infected area by means of a rigid quarantine. Transmission of the contagium has occurred through the bedding, clothing, and other effects of patients. The corpses of persons who had died of the plague have been known to transmit the infection, even when a long time had elapsed after death. This fact was recognized ages ago in some of the

Eastern countries, and consequently the reopening of graves of persons who had died of the plague was made a penal offence. "Such graveyards were therefore frequently surrounded with walls, upon which notices were posted to the effect that the reopening of a grave would be punished as a capital offence."[1]

It would seem that the poison of the plague is capable of remaining for a long time in an active state outside of the body, as epidemics not infrequently break out anew after a long interval and without any fresh importation of the infection. The contagium of the plague is believed to enter the system usually through the lungs. A few instances are recorded showing that it is possible to produce the disease by inoculation. The presence of the infection in the circulation is first manifested in the lymphatic system, causing swelling and inflammation of the glands.

The stage of incubation is short, being usually from two to five days. It may, however, be as long as seven or eight days, but rarely longer.

PATHOLOGICAL ANATOMY.—The gross pathological changes are not numerous: no careful examination has ever been made of the blood. Swelling and inflammation of the lymphatic glands are the only constant abnormal changes found after death. The inflammation is not always limited to the glands, but extends more or less to the contiguous tissue, in which extravasation of blood is often found. More often the inguinal glands are the ones involved, although it is not unusual to find glandular swellings in the axilla, the neck, and other external portions of the body. The deep seated lymphatic glands, and even those within the cavities of the body, are also not infrequently enlarged. The external glands, especially those in the inguinal region, are very liable to undergo suppuration. When those in the axilla are severely involved the inflammation sometimes extends to the pleura.

Petechiæ, ecchymoses, and carbuncles are frequently found in the skin. The carbuncles often present large sloughs, surrounded, of course, by an inflammatory process. Ecchymoses are sometimes found in the mucous and serous membranes. Parenchymatous degeneration has been noticed in the various internal organs of the body: the spleen, especially, is said to be almost always hypertrophied, soft, and of dark color (Liebermeister).

SYMPTOMS.—In studying the symptoms of the plague it is found most convenient to divide the disease into four stages: First, the prodromal or invasive stage; second, the febrile stage; third, the stage of the local manifestations; fourth, the stage of convalescence.

First Stage.—The disease usually begins somewhat suddenly by feelings of lassitude, loss of strength, general uneasiness, and mental anxiety. Headache is commonly present, together with vertigo and a sense of fulness in the head. The face is generally pale, the eyes languid, the intellectual faculties impaired, and the gait unsteady or staggering, resembling that of an intoxicated person. It is not unusual to find nausea and vomiting, and even diarrhœa, at this stage. These early symptoms may be either very mild or very severe, and may continue from a few hours to two or three days. During this period there is usually but little if any fever.

The *second stage* is ushered in by chilliness or rigors, followed by febrile reaction. There is a continuance of most of the symptoms already mentioned, some of which may assume still greater prominence—such as the languor, debility, headache, dizziness, and the irritability of the stomach. Precordial uneasiness is very commonly complained of. The fever often becomes very intense. It is not unusual to find the temperature of the body rise as high as 104° F., but more frequently it ranges between 101° and 104° F. There are present also the usual concomitant symptoms of high fever, such as a hot and dry skin, unquenchable thirst, furred tongue, and accelerated respirations. The pulse is not only frequent, but feeble, and sometimes irregular or intermittent. In severe cases it may vary from 120 to 150. The tongue at first is somewhat swollen, moist, and covered with a white fur, but later it becomes brown or almost black, and sometimes fissured, while dark sordes collects on the teeth and lips. The eyes are injected, the face flushed or livid, and the countenance is greatly changed. At first the bowels are constipated, but toward the end are relaxed, the passages becoming dark, offensive, and sometimes bloody. A dark grumous or bloody vomit is not uncommon. The urine also is often tinged with blood. When these symptoms are present the patient soon sinks into a typhoid condition; delirium, stupor, or profound coma supervene, and death often results about the time the lymphatic glands begin to enlarge.

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[1] Liebermeister, *v. Ziemssen's Cyclopædia.*

In the most malignant cases the fatal blow appears to be given at the very commencement of the disease. Such cases are characterized by severe nervous symptoms and extreme prostration, from which the vital forces never rally, and death often results in less than twenty-four hours without any development whatever of the local manifestations.

Usually the febrile symptoms are not of uniform violence throughout the twenty-four hours, but there are remissions and exacerbations. The remissions occur in the morning and toward evening, the exacerbations in the middle of the day and at night. The morning remission and the nocturnal exacerbation are most marked. The remission is often so great as to lead the patient to hope that convalescence has begun. The subsidence of the fever is not infrequently attended with free perspiration, and when this occurs on the third or fifth day of the disease it is regarded as a favorable indication. After the febrile symptoms have continued for two or three days the inguinal lymphatic glands enlarge and become sensitive to pressure. The intensity of the fever now diminishes, although the temperature often fluctuates considerably throughout the succeeding stage.

The *third stage* is characterized by the development of the local lesions. Usually the earliest evidence of localization of the disease is found in the inguinal region, and consists of inflammation and swelling of the lymphatic glands. This symptom is often preceded by a shooting pain in the part. Next to this region, the glands in the axilla are most frequently affected. Those in the neck, and even in other parts of the body, are often attacked in severe cases. The swellings vary very considerably in size. Sometimes they are so small as to be difficult of detection; in other cases they become as large as a hen's egg or even much larger. In the neck the swelling has been known to attain enormous dimensions within a few hours, becoming so large, indeed, as to cause asphyxiation from pressure. The swelling, however, is apt to be greatest in the inguinal region, and the glands which are attacked are usually those lower down on the thigh than in the case of venereal buboes. Suppuration may occur, or the inflammation may disappear by resolution. The former is thought to be the more favorable mode of termination. The suppurative process is apt to be slow, continuing often as long as two or three weeks before the pus is discharged. After this the abscess slowly heals, leaving a permanent scar.

Carbuncles, which are less frequent than buboes, usually make their appearance at a later period. They may appear upon any part of the body, but are more often found on the lower extremities, the buttocks, and the back of the neck. Sometimes there is but one or there are very few, and at other times they are quite numerous. They may be either small or large. In favorable cases, instead of gangrene developing, which is often the case, the slough separates early by suppuration.

Petechiæ, vibices, or extensive ecchymoses are often seen in the last stage of fatal cases. Aubert regarded these symptoms as almost a certain sign of death.

It should be stated that it is not possible in every case of the plague to find clearly marked the three stages just described. Sometimes the first symptom that attracts attention is a so called "boil," which has made its appearance without premonition. Occasionally the disease is so mild that the patient is not obliged to go to bed. Such cases may be seen in mild epidemics or toward the close of severe ones. On the other hand, in the most severe form of the disease cases have been known to terminate fatally within a few hours, without any appreciable preliminary symptoms. In this class of cases death results from shock produced by the virulence of the poison. More frequently, however, in the fatal cases death takes place between the third and fifth days. After the eighth or ninth day, or even after the seventh according to Liebermeister, the dangerous period of the disease is past, yet death may result from sequelæ. The subsidence of the fever on the third or fifth day, with profuse perspiration, as already mentioned, is regarded by most observers as favorable.

Fourth Stage.—In most of the cases which terminate favorably convalescence begins from the sixth to the tenth day, but, on account of the suppuration and a large number of discharging sinuses, is often very slow. During this stage certain sequelæ are liable to arise, among which may be mentioned furuncles, secondary abscesses, parotitis, dropsy, partial paralysis, and mental disturbances. Pneumonia, attended by a typhoid condition, is sometimes seen, and when it occurs is always very fatal. In pregnant women abortion is apt to take place, and this complication is almost always followed by death. A genuine relapse has been known to occur when convalescence seemed fully established.

DIAGNOSIS.—It is difficult to distinguish the plague only at the beginning of an epidemic or in cases which are atypical. When the disease is known to be prevalent the diagnosis in well marked cases is usually easy enough. Some doubt might exist in the mind of the diagnostician during the first day or two of the illness, but the early appearance of shooting pain in the inguinal region, rapidly followed by tenderness and swelling of the glands and the formation of buboes, is calculated to reveal the true nature of the disease; but if any doubt should still exist, it would soon be removed by the rapid spread of the malady, the development of carbuncles and petechiæ, and the frightful mortality.

The diseases with which the plague is most liable to be confounded are lymphadenitis, scrofulous or syphilitic affections associated with fever, malignant typhus, pernicious paludal fever, and malignant pustule. But a reasonable familiarity with the symptoms of these diseases will usually enable the diagnostician to exclude them when considering the differential diagnosis between them and the plague.

PROGNOSIS.—As the plague is an exceedingly fatal disease, the prognosis in well marked cases should be guarded. Some idea of the great fatality of the disease may be formed by considering the results of certain epidemics. For example, it was estimated that in Marseilles in 1720, out of a population of 90,000, 80,000 suffered from the disease, and of this number 40,000 perished. Likewise, in Toulon in 1721, out of a population of 26,000, about 20,000 took the disease, and of these 16,000 died. Also, in Moscow in 1770–71, nearly one-half of the entire population perished. In various epidemics the death rate among persons attacked has ranged from 50 to 90 per cent.

In individual cases the unfavorable symptoms may be enumerated as follows: sudden and extreme prostration at the onset; a tendency to syncope, stupor, or coma; injected eyes, stammering speech, unsteadiness of gait, and a drunken expression; a low muttering delirium; excessive oppression of breathing, and an irregular or intermittent pulse; a dry, black tongue; hiccough, severe precordial pain, and vomiting of dark grumous material; the appearance of petechiæ, vibices, and large ecchymoses. On the other hand, the favorable symptoms are early and decided remissions in the fever, and its subsidence on the third or fifth day, with moderate perspiration; a limited involvement of the lymphatic glands; the development of buboes, advancing rapidly to suppuration; no great loss of strength; the cessation of the nervous symptoms; and a return of the natural expression of the countenance.

TREATMENT.—It is sometimes easier to prevent than to cure a disease, and this is particularly true of the plague; for it is certain that a great deal may be accomplished in the way of prophylaxis by suitable measures energetically applied, while it seems impossible to change the course of the disease after symptoms have appeared. Some of the severest epidemics of this disease have not only been limited in their spread, but were conquered by quarantine and hygienic measures.

The history of the latest epidemics in Egypt is very instructive as showing what may be accomplished by a rigid quarantine system. The importance of this measure was also very forcibly demonstrated at Noja, Italy, when the plague prevailed there in 1815. The city was surrounded by three separate military cordons, one outside of the other, thus preventing absolutely any person from either entering or leaving the infected locality, and, as a result, the disease was confined within the limits of this *cordon sanitaire*. It is reasonably believed that by this severe measure Lower Italy, and even Europe, were spared from the decimating ravages of the scourge. So also in the province of Astrakhan in 1878–79 the plague was prevented from spreading by the same rigid restrictions.

A writer[1] who is thoroughly familiar with the history of this disease says: "The extinction of the plague was a gradual process, and kept pace in great measure with the development and perfection of the quarantine system as carried out, not only with reference to the East, but also between neighboring countries of Europe. Indeed, I cannot understand how any one pretending to criticise facts in an unprejudiced manner, and with some regard to the condition of the plague in the East, can for a moment hesitate to attribute the chief cause of the disappearance of the plague from European soil to the development of a well regulated quarantine system."

Under the head of Etiology (page 392) attention has been directed to the fact that poverty, overcrowding, bad ventilation, unwholesome or insufficient food, and unhealthy surroundings are important factors favoring the propagation and dissemination of the infection. It is evident, therefore, that in the administration of sanitary laws these conditions should receive attention. Exposed persons should not only be properly fed and have their dwelling rooms well ventilated, but they should bathe regularly and avoid intemperate and all other depressing habits. It is clearly the duty of the state or municipality in which the disease exists to correct all bad hygienic conditions or unsanitary surroundings. The polluted soil should be saturated, if possible, with some active disinfectant; all articles of clothing, bedding, etc. which have been in contact with the sick should be promptly disinfected, as well as the dwelling in which the patient resided. The bodies of persons having died of the plague should be buried in accordance with strict sanitary regulations, or, preferably, reduced to ashes speedily by the process of incineration.

Clinically considered, there is no special form of treatment for the plague: all that can be done is to treat the symptoms as they arise. The fever may be mitigated by febrifuge mixtures or some of the least depressing antipyretics of the coal-tar products. Cold sponging, or even cold baths, may prove of great service when the temperature is high. As suppuration of the buboes is thought to be desirable, this process should be encouraged by warm poultices, and as soon as pus has formed it should be evacuated and the parts treated in accordance with antiseptic principles. The danger of collapse in the early stage of the disease may be lessened by confining the patient to bed and instituting at once a supporting plan of treatment. As death is generally caused by cardiac paralysis, strychnine and alcohol should be given in large doses. A liberal amount of suitable nourishment is required.

[1] Hirsch, quoted by Liebermeister, *loc. cit.*

INFLUENZA.

By JAMES C. WILSON, M. D.

Definition.—An acute infectious disease occurring in widely extended epidemics, characterized by catarrh of the mucous membranes of the respiratory tract, less frequently of the digestive tract, by quickly oncoming debility, and by nervous symptoms. There is a strong tendency to complications, especially pneumonia. Uncomplicated cases are rarely fatal except in feeble or aged persons. The attack does not confer subsequent immunity.

Synonyms.—Epidemic catarrhal fever; la Grippe. This disease has an extensive literature and innumerable synonyms. Many of these terms are the outcome of efforts on the part of the profession to give it descriptive designations; others are of popular origin, suggested by its sudden occurrence, certain of its symptoms, or its widespread prevalence. The Russians have called it Chinese catarrh; the Germans and Italians, the Russian disease; the French, Italian fever or Spanish fever. In two instances the popular name has found its way widely into medicine and medical literature almost to the exclusion of the studied terms by which science has sought to designate it. These are influenza and la grippe.

The derivation of la grippe is obscure. It has been traced to the Polish *chrypka* (raucedo); others have derived it from *agripper* (to snatch). The term influenza is of Italian origin. It is said that the disease received this name because its sudden outbreak and wide prevalence were attributed to some influence of the stars, or, according to others, from a secondary signification of the word indicating something fluid, transient, or fashionable.

History.—Influenza is distinctly an epidemic disease. It has prevailed since the beginning of the sixteenth century in great pandemics. Many of the accounts of epidemic diseases of earlier date doubtless refer to influenza, but they are not sufficiently exact to warrant us in inferring its undoubted existence. According to Parks, it is mentioned in the writings of Hippocrates, who, however, gives no exact description. Several epidemics of catarrhal fever, Italian fever, and the like, which were probably influenza, occurred in the ninth century. In the year 827 A. D. a cough which spread like the plague was recorded. In 876 there appeared in Italy a similar epidemic which spread with great rapidity all over Europe. In 1173 a widespread malady, of which the symptoms were chiefly catarrhal, raged throughout Europe, and epidemics of a like character occurred during the following century (1239–99). There are to be found records of six similar epidemics in the fourteenth century, and seven great visitations of influenza occurred in the fifteenth century. Aitken[1] speaks of a very fatal prevalence of influenza throughout France in 1311, and of an epidemic in 1403 in which the mortality was so great that the courts of law in Paris were closed in consequence of the deaths.

The earliest accurately described epidemic of the British islands is that of the year 1510. The disease apparently started from Malta, invaded Sicily, then Italy, Spain, and Portugal, then crossed the Alps into Hungary and Germany, extending westward into France and Britain. Its track widened over all Europe from the southeast to the extreme northwest, and it is said that not a single family and scarce a person escaped it. It was attended by "a grievous pain in the head, heaviness, difficulty of breathing, hoarseness, loss of strength and appetite, restlessness, retchings from a terrible tearing cough. Presently succeeded a chilliness and so violent a cough that many were in danger of suffocation. The first day it was without spitting, but about the seventh or eighth day much viscid phlegm was spit up. Others (though fewer) spat only water and froth. When they began to spit, cough and shortness of breath were easier. None died except some children. In some it went off with a looseness, in others by sweating. Bleeding and purging did hurt" (Thomas Short).

The epidemic of 1557, starting westward from Asia, spread over Europe, and then crossed the Atlantic to America. The malady broke out in England in the month of September. "Presently after were many catarrhs, quickly followed by a more severe cough, pain of the side, difficulty of breathing, and a fever. The pain was neither violent nor pricking, but mild. The third day they expectorated freely. . . . . Some, but very few, had continued fevers along with it; many had double tertians; others simply slight intermittent. All were worse by night than by day; such as recovered were long valetudinary, had a weak stomach and hypped." Gravid women either aborted or died. This epidemic spread with frightful rapidity. Thousands were attacked at the same time. The entire population of Nismes, with scarcely an exception, fell ill with it upon the same day. It was extremely fatal. The disease raged in some parts until the middle of the following year (1558), and carried off in Delft alone five thousand of the poor. In all cases mild treatment was called for, with warm broths and speedy immersals, "to recall the appetite and keep the vessels of the throat open."

About a quarter of a century later, in 1580, a great epidemic of influenza spread from the southeast toward the northwest, over Asia, Africa, and Europe from Constantinople and Venice, and extended over Hungary and Germany to the farthest regions of Norway, Sweden, and Russia. It prevailed in England, and was described by Dr. Short. In Italy it was rife during August and September, in England from the middle of August to the end of September, and in Spain during the whole summer. In most places its duration was about six weeks. The termination was, as a rule, favorable. In the account of Dr. Short it is stated that "few died except those that were let blood of or had unsound viscera." In some districts, on the contrary, the course of the disease was very severe. In Rome two thousand died of it, according to the author just cited, but Zuelzer states that victims of the epidemic in the Eternal City numbered not less than nine thousand, and adds that Madrid must have been almost depopulated by it.

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[1] *Practice of Medicine.*

This high mortality has been attributed to the bloodletting practised in the treatment of the disease. The symptoms are similar to those of the previous epidemics, with great shortness of breath, which continued in many cases some time after the disappearance of the catarrhal trouble.

Influenza reappeared in Germany in 1591. An epidemic extending from Holland through France and into Italy occurred in 1593. In 1610 catarrh prevailed throughout Europe. In 1626–27 epidemic catarrhal fever made its appearance in Italy and France; in 1642–43, in Holland; in 1647, in Spain and the colonies of the Western World; and again in 1655 in North America. Noah Webster, in his work entitled *A Brief History of Epidemic and Pestilential Diseases*, published in London in 1800, states that the outbreak of 1647 was the first epidemic of catarrh mentioned in American annals. Epidemic catarrh revisited Austria, Germany, and England in 1658 and again in 1675. The first of these two epidemics is described by Willis, the second by Sydenham, as they occurred in England, and the accounts are to be found in the *Annals of Influenza*. About this time the disease began to be known as influenza, and it is interesting to note that the influence of the stars suggested itself in connection with its sudden appearance and wide prevalence. Willis writes that "about the end of April (1658) suddenly a distemper arose as if sent by some blast of the stars, which laid hold of very many together—that in some towns in the space of a week above a thousand people fell sick together."

Epidemics occurred in Great Britain and Europe in 1688, 1693, and in 1709. Epidemic catarrh spread in 1712 widely over Europe from Denmark to Italy. In 1729–30 a great epidemic swept over Europe. In five months the disease overspread Russia, Poland, Germany, Sweden, and Denmark. In Vienna sixty thousand persons fell ill of it. In the autumn it reached France and Switzerland and extended to England; it extended to Italy, thence to Spain, from which country it found its way to Mexico. The symptoms were those already described as characterizing the attack in previous epidemics. The attack began with pains in the limbs, and fever, hoarseness, catarrh, dyspnœa, and cough followed. Delirium, drowsiness, and faintness occurred in some cases. Turbid urine, copious sweating, looseness of the bowels, and nosebleeding were common. In Switzerland only children and old persons died. In this pandemic the disease was not very fatal.

Influenza invaded Saxony and Poland two years later, and, spreading through Germany, Switzerland, and Holland, reached Great Britain in December, 1732. Thence, toward the end of January, it spread to France, Italy, Spain, and westward to North America, passing on to the islands of the West Indies and to South America. The disease in this epidemic ran a favorable course, the attack terminating in from three to fourteen days, with sweating, bleeding from the nose, or an abundant discharge from the nasal passages. The aged and those suffering from chronic pulmonary disease mostly perished. In Scotland three forms of the attack were described—the cephalic, the thoracic, and the abdominal. This pandemic slowly extended over Eastern Europe and lasted until 1737. It is of this outbreak that John Huxham of Plymouth wrote as follows: "About this time a disease invaded these parts which was the most completely epidemic of any I remember to have met with; not a house was free from it; the beggar's hut and the nobleman's palace were alike subject to its attacks, scarce a person escaping either in town or country; old and young, strong and infirm, shared the same fate." . . . . "The disorder began at first with a slight shivering; this was presently followed by a transient erratic heat and headache and a violent and troublesome sneezing; then the back and lungs were seized with flying pains, which sometimes attacked the heart likewise, and, though they did not long remain there, yet were very troublesome, being greatly irritated by the violent cough which accompanied the disorder, in the fits of which a great quantity of thin, sharp mucus was thrown out from the nose and mouth. These complaints were like those arising from what is called catching cold, but presently a slight fever came on, which afterward grew more violent; the pulse was now very quick, but not in the least hard and tense like that in a pleurisy; nor was the urine remarkably red, but very thick and inclining to a whitish color; the tongue, instead of being dry, was thickly covered with a whitish mucus or slime; there was an universal complaint of want of rest and a great giddiness. Several likewise were seized with a most racking pain in the head, often accompanied by a slight delirium. Many were troubled with a tinnitus aurium, or singing in the ears; and numbers suffered from violent earaches or pains in the meatus auditorius, which in some turned to an abscess. Exulcerations and swelling of the fauces were likewise very common. The sick were in general very much given to sweat, which, when it broke out of its own accord, was very plentiful and continued without striking in again, and did often in the space of two or three days wholly carry off the fever. You have here a description of this epidemic disease such as it prevailed hereabouts, attacking every one more or less; but still, considering the great multitude that were seized by it, it was fatal to but few, and that chiefly infants and consumptive old people. It generally went off about the fourth day, leaving behind a troublesome cough, which was very often of long duration, and such a dejection of strength as one would hardly have suspected from the shortness of the time.

"On the whole, this disorder was rarely mortal, unless by some very great error arising in the treatment of it; however, this very circumstance proved fatal to some, who, making too slight of it, either on account of its being so common or not thinking it very dangerous, often found asthmas, hectics, or even consumptions themselves, the forfeitures of their inconsiderate rashness."

Widely extended epidemics prevailed in Europe and America in quick succession between the years 1737 and 1780. One of the most remarkable epidemics of this disease is that described as the epidemic of 1782. It came from the East, from Asia into Russia. From St. Petersburg it spread during the winter and spring over Sweden, Germany, Holland, and France; in the autumn it showed itself in Italy, Spain, and Portugal. In Vienna three fourths of the population fell ill of it so suddenly that it for the first time received its appellation "Blitz catarrh."

Numerous outbreaks of influenza occurred in Europe and America during the years 1788–90. One of these has been well described by Dr. John Warren of Boston in a letter to Lettsom. This letter is dated May 30, 1790, and among other matters of great interest respecting the disease it is stated that "our beloved President, Washington, is but now on the recovery from a very severe and dangerous attack of it in that city" [New York]. No great epidemic followed until 1798, when the malady again showed itself in Russia and spread over the greater part of Europe, continuing to prevail in various parts until 1803.

In the year 1830 influenza again became pandemic. It showed itself first in China; in September it reached the Indian Archipelago, invaded Russia, and reached Moscow in November, whence it spread rapidly to Poland, Prussia, Denmark, Finland, and Germany. By June it had reached England, sweeping southward in the early winter into Italy and westward across the Atlantic to North America, where it still prevailed in various regions in the United States at the close of the winter of 1831–32. Meanwhile it continued in the East.

In June, 1833, it again showed itself in Russia, and repeated its wanderings as before. From 1837 to 1851 numerous epidemics took place. The epidemic of 1847–48 has been described by many writers, and, with much exactness as it occurred in London, by Peacock. It is estimated that one fourth of the entire population of that city were affected by the disease. The epidemic prevailed in London for six months, and it is interesting to note that although the deaths registered for the entire period as from influenza amounted to only 1739, the report of the Registrar General showed that during the six weeks the epidemic was at its height not less than five thousand persons died in the metropolitan districts in excess of the average mortality of the period, the increased death rate showing itself in nearly every class of disease, the local maladies which had been the prominent affection being doubtless in many cases assigned as the cause of death.

Influenza prevailed over a wide area of the United States during the early months of 1879.

From the time of the great epidemic of 1847–48 the disease affected a smaller proportion of the inhabitants of the localities in which it appeared, and proved a comparatively unimportant malady. For this reason it for many years occupied a less conspicuous place in medical literature.

In 1889 influenza again appeared in the form of a veritable pandemic. It first showed itself early in the spring in the steppes of Tartary, appearing in Bokhara in May. It advanced thence by two routes—eastward toward the Chinese Empire, and westward over Russia and Europe to the United States. Scattered cases showed themselves in New York and Philadelphia about the middle of December. In a few days the disease became epidemic, and prevailed very generally in the Eastern cities during the last week of the year. It spread with great rapidity throughout the United States. In April, 1890, it had reached Mexico, New Zealand, Australia, and South America. In many of the infected regions the disease has prevailed with great intensity, the larger number of the inhabitants being affected. It has subsided only to recur at irregular intervals with gradually diminishing intensity until the present time (autumn, 1896).

During this period influenza has again become a familiar disease and has been carefully and thoroughly studied. On the one hand, many of the popular delusions and professional conjectures in regard to it have been dispelled, while, on the other, some of the shrewd observations of the older practitioners have been confirmed. The bacterial nature of the infecting principle has been demonstrated. From the date of the present pandemic the disease takes its proper nosological position among the acute infectious maladies. Much work, however, remains to be done. Where and under what conditions the infecting principle originates, and what the influences may be that from time to time call it into activity and send it forth in definite directions over the earth, are yet unknown.

Catarrhal affections have frequently prevailed among domestic animals during epidemics of influenza. Horses, dogs, and cats have manifested these disorders. Neat cattle and sheep have been less commonly affected. These epizoötics have in some instances preceded the outbreak of influenza among men; in other instances they have appeared at the same time; while in a widespread outbreak among horses in the United States in 1872 the disease did not affect man except to a limited extent. In 1880 in the United States, following an outbreak of influenza among men, an extensive epizoötic, chiefly affecting horses, prevailed in Canada and the United States east of the Mississippi River.

ETIOLOGY.—1. *Predisposing Influences.*—When the disease invades a community a large proportion of the population is attacked without distinction of age, sex, social condition, or occupation. Previous illness affords no protection. Aged and infirm persons and those of nervous temperament are peculiarly liable to suffer, but the robust possess no immunity. All races and dwellers in every climate are liable to the attack. Upon the outbreak of an epidemic adults are attacked earlier than children. In some epidemics children have manifested a slight relative immunity.

Influenza is not self-protective. An attack confers no exemption from the disease in subsequent outbreaks, and independently of relapses, which frequently occur, individuals have been known to experience a second attack during the prevalence of the same epidemic. Local unhygienic conditions favor the prevalence of the disease in its more severe forms, and the increase of the death rate during outbreaks of influenza is proportionately greater in districts in which there is ordinarily a high mortality as compared with healthier places. Influenza bears no relation with known atmospheric conditions. It prevails at all seasons of the year, and is in no way dependent upon low temperature nor abrupt changes of the weather. It has prevailed in very high latitudes and at all altitudes. Epidemics have recurred at irregular periods. It was at one time thought that the disease recurred in cycles of about one hundred years. This view is unsupported by the facts. A review of the history of the subject shows, however, that at intervals of twenty-five to forty years great epidemics have swept over vast areas of the earth's surface, while more limited outbreaks have occurred with greater or less frequency in the years succeeding the pandemics. It does not, however, appear possible to establish anything like a regular periodicity in the return of the disease.

The great epidemics have in most instances spread in a direction from the east or northeast toward the west and south. On other occasions they have taken the opposite course, and sometimes they have appeared to radiate in various directions from several centres. In consequence of these facts two views have arisen concerning the origin of the affection: First, that each epidemic starts out from some single unknown source and spreads thence from point to point, invading more distant localities successively as it advances, until at length it dies out in regions remote from the starting point. It in no wise conflicts with this view that outbreaks recur from time to time in the regions thus successively invaded. The second view is that influenza arises not from some single particular place, but that the infecting principle is widespread in nature, and called into activity from time to time by unknown atmospheric or telluric causes, and that the great epidemics, being made up of successive outbreaks of the disease, have many distinct points of origin.

The progress of influenza from place to place has usually been rapid. In this respect, however, the epidemics have shown great diversity. The disease has sometimes travelled slowly. It is said to have overrun Europe in six weeks, and on other occasions it has occupied six months in doing so. It has sometimes attacked regions widely remote from each other within short intervals of time, and has appeared at the same time in different quarters of the globe. A careful study of the facts relating to the recent pandemic shows that influenza follows the lines of travel and advances at about the ordinary rate of commercial intercourse. The mere fact that the disease, first noted in Central Asia in the spring of 1889, extended westward toward Europe and eastward toward China serves to explain its simultaneous appearance in distant quarters of the globe. The well established fact that the infecting principle may be transmitted by fomites renders intelligible at least the occasional outbreaks at sea and at distant points where the disease had not previously prevailed in the ordinary manner.

When influenza develops in a community it continues to prevail, as a rule, from four weeks to two months, exceptionally for a much longer time. The epidemic of 1831 was continuously prevalent in Paris for nearly a year. The epidemics are occasionally heralded by scattered cases. More commonly the disease attacks almost simultaneously great numbers of inhabitants of infected districts, so that when the epidemic is severe the sick may be soon counted by thousands and business is sometimes seriously interfered with. The epidemics rapidly reach their height, and usually subside almost as suddenly as they began. During the prevalence of the disease since the winter of 1889–90 scattered cases and groups of cases have occasionally occurred in the intervals between the recurring annual outbreaks. In large cities the disease makes its appearance nearly at the same time in several different localities, and spreads from these as foci of infection throughout the entire community. Cities and large towns are generally affected earlier than the villages surrounding them.

2. *The Exciting Cause.*—Among the questions finally settled by a study of the disease in the recent epidemic is that of its contagiousness.

Influenza is highly contagious, and extends by direct or indirect communication from the sick to the well. Until recently the view was almost universally held that the cause of the disease was miasmatic in its nature and spread independently of direct contact. It is interesting in this connection to note that Haygarth, writing of the outbreaks of 1775 and 1782, declares as the result of his observations that the influenza spreads "by the contagion of patients in the distemper;" and Falconer, writing of the epidemic of 1803, says, "I have no doubt that it is contagious in the strictest sense of the word."

The following personal observation is in accord with the general experience of recent times: In the first days of an outbreak of influenza a physician was called in the evening to see the child of a medical friend. The little patient, who had been sick two days, was supposed to be developing enteric fever. It subsequently proved that he had influenza, which rapidly attacked every member of the household. The physician called in consultation spent twenty minutes at the bedside of the patient, going over the history of the case and making a careful physical examination. Twenty four hours later he developed a violent attack of influenza which confined him to his bed for a week.

That the belongings of the patient may constitute fomites and the corpse itself prove a source of infection is established by the observation of White and Guitéras in regard to a localized outbreak in a remote community in 1880. These observers have placed upon record the following circumstance: "Influenza prevailing in Europe, an American gentleman in bad health contracted the disease in London; improved; suffered a relapse in Paris, and died there at the end of September, 1879. His body was embalmed and sent home. Following the exposure of the remains of this person to the view of his family there was an outbreak of influenza with characteristic symptoms which affected, first, members of that family; next, friends living in close association with them; next, the medical attendant of some of them; and finally, the housekeeper and one or two patients of one of the physicians who wrote the paper, the whole number being about twenty cases."

In the spring of 1892, Pfeiffer, at the Hygienic Institute of Berlin, succeeded in isolating among the micro-organisms found in the nasal and bronchial secretions of patients suffering from influenza a bacillus which he regards as characteristic. This micro-organism is a short rod about one half the length and nearly the same thickness as the bacillus of mouse-septicæmia. It is non-motile; it stains in Löffler's methylene blue or Ziehl's carbol-fuchsin, and presents the appearance of two bulbous ends joined by a narrower and less deeply stained central portion. It occurs in great numbers in the nasal secretions, and is frequently seen in the sputa almost in pure culture. At the close of the attack the bacilli become relatively few in number, but persist for some time after the subsidence of active symptoms. Kruse states that in doubtful cases the diagnosis of influenza can be established with certainty and without difficulty by an examination of the sputum. Cover-glass preparations are stained with a dilute pale red solution of carbol-fuchsin in water, and the bacilli may be readily recognized. This bacillus was demonstrated by Canon in the blood of a series of consecutive cases at the Moabit Hospital of Berlin. The cultures have been grown in agar containing a small amount of sugar. It grows with difficulty in bouillon, which remains clear. It requires for its culture a temperature which liquefies gelatin. It grows best on culture media in which hæmoglobin is present. Inoculation experiments have been, as a rule, successful, though Voges failed to produce influenza in the lower animals with Pfeiffer's bacillus. Pfeiffer was able to demonstrate the presence of this bacillus in all cases of true influenza examined. It is not found in other diseases. It must thus be regarded as characteristic.

The disease is communicated from the sick to the well by direct contact and close association. It is probable that the infecting principle, like that of measles and pertussis, is inhaled with the inspired air.

PATHOLOGICAL ANATOMY.—Uncomplicated influenza is rarely fatal. As a rule, the unfavorable termination is due to lung complications. The lesions are congestion and catarrhal swelling of the mucous membrane of the upper air-passages and the bronchial tubes. These lesions may be restricted to the trachea and larger bronchi or extend to the finest twigs. They may consist of great thickening and deep capillary injection of the mucous lining of the tubes, which contain clear frothy mucus or thick viscid masses of muco-purulent secretion unmixed with air. The bronchial glands have been found to be enlarged and softened. A catarrhal condition of the mucosa of the stomach and intestines has been observed. The mesenteric glands may be slightly enlarged. The spleen has been found moderately enlarged.

SYMPTOMS.—*General Description of the Disease.*—Influenza in individual cases presents the widest variation as regards intensity, from a trifling indisposition to an illness of the gravest kind, which may terminate in death. In this respect, with the exception that the range of variation is greater, influenza resembles other acute infectious diseases. The variations are, however, to some extent related to, first, the previous health of the individual, his age, and the power of resisting morbid influences which he possesses; second, the character of the prevailing epidemic.

Cases of great severity are occasionally observed during the prevalence of mild epidemics. In every epidemic, however, the majority of the sufferers manifest the disease in a mild form, very many in what may be termed a rudimentary form.

The period of incubation is brief, varying from a few hours to two or three days. This period is usually unattended by subjective symptoms.

The onset of the attack is abrupt, and in most instances is marked by chilliness or a chill of moderate severity, which may be prolonged and repeated; fever rapidly supervenes. There is headache, usually severe, with pain back of the eyeballs, severe pain in the back, limbs, and joints, and a general feeling of soreness, with tenderness upon pressure. These symptoms are accompanied by mental and physical depression, with malaise and restlessness. The forces of the circulation are notably depressed. The spleen is slightly enlarged. There is no characteristic eruption. The duration of the attack is from three or four to seven days, and the patient only slowly regains his habitual physical and mental vigor.

In mild cases the chill may be slight, transient, or absent altogether. The headache and muscle pains are of moderate intensity. There is malaise; weariness upon bodily and mental effort; disinclination for affairs; some difficulty in fixing the attention; and not infrequently slight mental confusion. To these nervous disturbances are added catarrhal symptoms, such as coryza and erythematous angina and a tickling cough. The fever is slight, the temperature not rising above 101° F., or the temperature may remain subfebrile throughout. A large proportion of the patients suffering from influenza in the milder form are able to continue their ordinary avocations. No very great degree of intensification of the symptoms is necessary, however, to compel the patient to betake himself to bed.

In the severer cases the chill is more marked, the shivering more prolonged. Fever is rapidly established, the acme being reached within twenty-four or thirty-six hours. The temperature may rise to 104–105° F. Sensations of heat alternate with chilliness. In many cases there are annoying sweats. Headache is intense; there is pain in the orbits and at the root of the nose. Sneezing, redness of the eyes and edges of the nostrils, a thin discharge from the nose, and lachrymation occur. Epistaxis is occasionally observed. The throat is sore; there is a tickling sensation in the upper air-passages, hoarseness, and sometimes dyspnœa. The cough is paroxysmal, distressing, and at first unproductive. It occasionally causes vomiting like that which occurs in the paroxysms of whooping cough. Chest pains, stitches in the side, loss of the sense of smell and of taste also occur.

The catarrhal symptoms in other cases are but slightly developed. The patient presents the symptoms of an acute infection of varying severity, beginning with chill and fever. There is great depression together with backache and pains in the limbs such as occur in dengue, with which influenza has been confounded, or variola. The appetite is lost; thirst, constipation, and diminished secretion of urine occur. The pulse may be full and compressible; more commonly it is feeble, small, and irregular. It is, as a rule, only moderately increased in frequency. In many cases there is slight blueness of the lips and finger tips; the patient is distressed by restlessness and want of sleep. At the end of four or five days the febrile symptoms decline, at times gradually, more commonly abruptly, and the defervescence is often accompanied by copious sweats, spontaneous diarrhœa, increased flow of sedimentary urine, and considerable amelioration of the subjective symptoms. The catarrhal symptoms outlast the fever two or three days, but cough and expectoration may persist for some time. During the attack there are evidences of a profound disturbance of the functions of the nervous system. There is depression alike of the body and mind, with mental dulness, and in some cases delirium. Slight convulsions may occur; cutaneous hyperæsthesia is often present, and areas of burning pain in the skin are encountered. Neuralgia, muscle pain, and aching referred to the bones are very common and often severe.

Symptoms referable to the nervous system may dominate the clinical picture from the onset or may become prominent at any time during its course. Blinding headache, intolerance of light and sound, intense rhachialgia may be associated with delirium and a tendency to stupor.

Painful rigidity of the muscles of the back of the neck and general convulsions may occur. There may be intense fever or the temperature may be subnormal, with slow, irregular pulse and respiration.

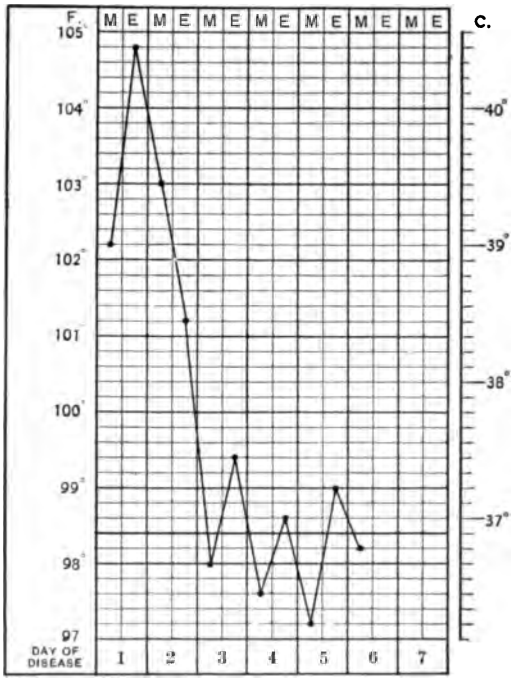
In other cases gastro-intestinal symptoms are prominent, while those referable to the respiratory system are less urgent. We observe nausea, occasional vomiting, a heavily coated tongue, complete inability to take food, gastric tenderness, slight tympany, and a tendency to diarrhœa. The attack may develop abruptly, with symptoms like those of cholera morbus. The fever and peculiar nervous depression are, however, the same.

Finally, cases occur in which there is but little of the usual tendency to localization of the infectious process; the patient suffers from fever of varying intensity, with great depression and simultaneous and equal implication of the respiratory, circulatory, nervous, and gastro-intestinal organs.

Herpes occurs in a considerable proportion of the cases. Urticaria is less common. Diffuse erythematous rashes and instances of purpura have been observed.

Attempts have been made to arrange the foregoing forms of influenza into different categories, and in theory a thoracic, cardiac, gastro-intestinal, and nervous variety may be recognized. In practice, however, the various described types merge so gradually into each other, and are so modified by the individual peculiarities of the sick and by the com-

FIG. 36.



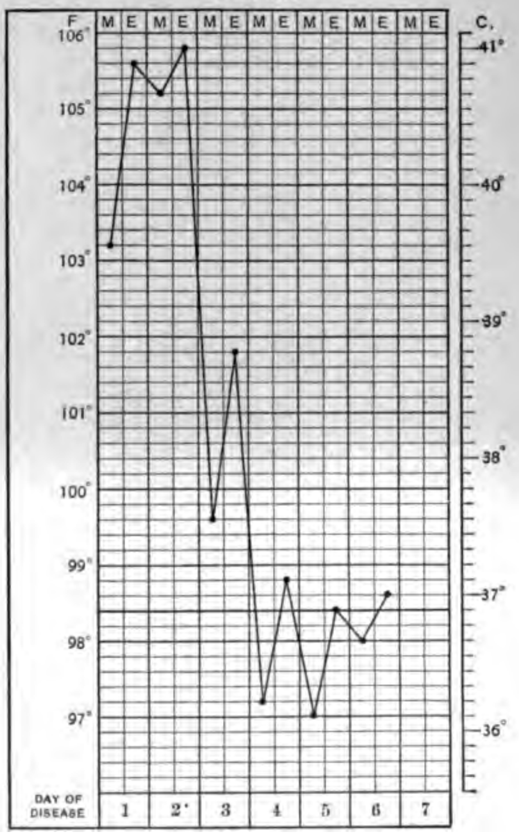
Temperature in Influenza—Critical Defervescence.

s v ch arise in the course of the attack, that there is, as a rule, le advantage in referring particular cases to theoretical categories.

DURATION of the milder forms of influenza is from two to three In well developed cases without complications convalescence sets n the fourth and seventh days. Severe cases with complica- y be protracted for several weeks. Relapses occur in about 10 cent. of the cases.

NALYSIS OF THE PRINCIPAL SYMPTOMS.—*The Fever.*—In un- plicated cases the temperature rises rapidly to 101–105° F. in the first twenty-four or thirty-six hours. From this point it falls by a defervescence usually critical; sometimes by an interrupted crisis; sometimes by rapid lysis. The temperature reaches the normal usually in the course of from one to four days; less commonly secondary rises of temperature occur after an afebrile period of one or two days—intermittent form; or, again, the fall of temperature does not reach the normal, and is succeeded by a series of rises, defervescence occurring some time before the close of the first week—remittent form. The accom-

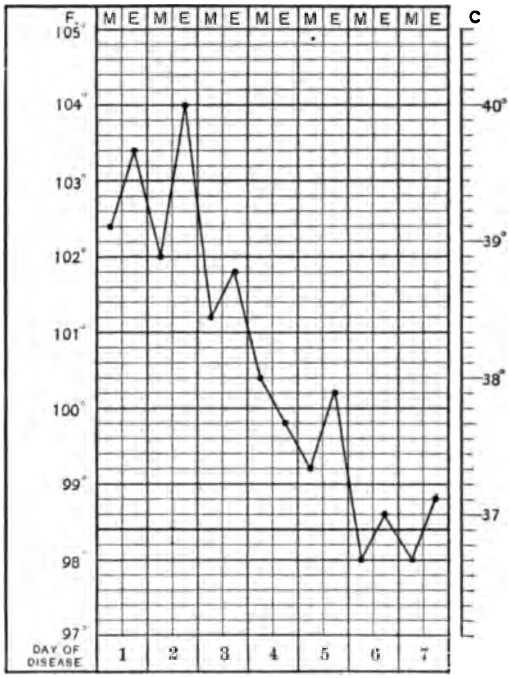
FIG. 37.



Temperature in Influenza—Interrupted Crisis.

panying charts represent the more common forms of the temperature curve. One recalls the statement of the chronicler of an early epidemic: "Some had continual fevers along with it; many had double tertians; others simply slight intermittent." There is no constant relation between the height to which the temperature rises and the severity of the other symptoms; subjective distress may be moderate in patients showing a temperature of 104–105° F., while other patients in whom the thermometer marks a fever of 101–102° F. may suffer agonizing pain in the head, back, and limbs. The temperature rises early in the course of the disease, and may subside before other characteristic phenomena show themselves; or, again, the temperature may be still high when the headache, pains, or even the catarrhal symptoms, have subsided. If the fever continue beyond the seventh or eighth day, it will usually be found, upon careful examination, to be due to some complication, as a rule involving the respiratory tract. The temperature curve, due to the influenza infection, not infrequently merges into that of a complicating bronchitis, broncho-pneumonia, or croupous pneumonia.

FIG. 38.

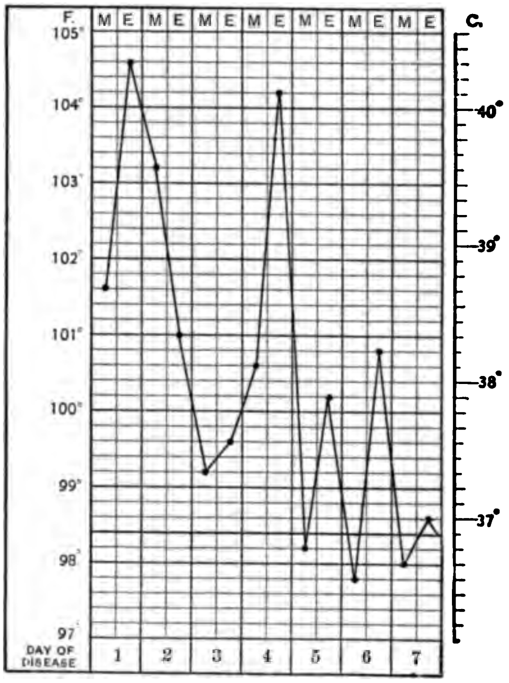


Influenza—Rapid Lysis.

The *pulse* has no constant characteristics. Its frequency is moderately increased; very often with high temperature the pulse does not exceed 100. It is less forcible than in health; compressible even when full; often irregular, changing in character in the course of a few hours. In some cases the pulse is slow.

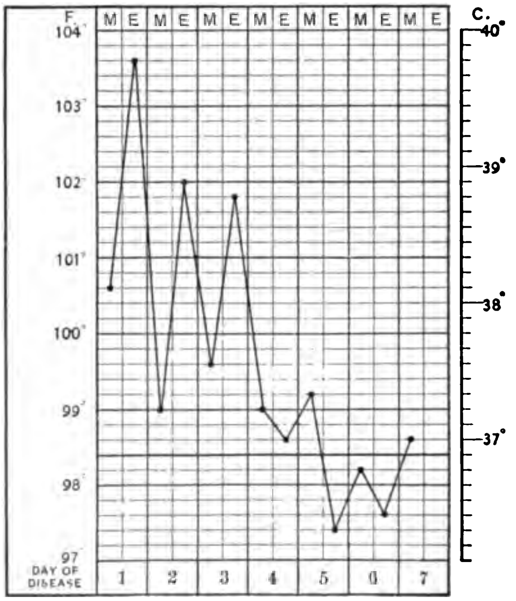
The *urine* is usually diminished, sometimes temporarily suppressed

FIG. 39.



Influenza—Intermittent Type.

FIG. 40.



Influenza—Remittent Type.

As a rule, it shows little change, and is not commonly, as in other febrile diseases, concentrated and high colored. It deposits on cooling a sediment of urates, which toward the end of the fever is often very abundant. Defervescence is in many instances attended by a copious excretion of urine. Albuminuria occasionally occurs, especially in complicated cases. Griffiths and Ladell isolated from the urine in influenza a toxic fever-producing ptomaïne which causes death in animals in eight hours. The substance was found to be a whitish crystalline body having the formula $C_9H_9NO_4$, soluble in water of slightly alkaline reaction.

The *skin* in some cases is hot and dry during the febrile movement; more commonly there is sweating from the onset, often continued through the course of the illness, and frequently being very marked during convalescence. Sudamina occur. The face is often flushed, and there are irregular erythematous mottlings of the skin, especially upon the neck and chest. Other forms of erythema, and especially erythema nodosum, have been frequently observed. Labial herpes is often seen in cases not complicated by pneumonia. Urticaria is not uncommon.

Disturbances of the digestive tract are more or less prominent in almost all cases. In many instances they are such as are usually seen in febrile disorders—namely, loss of appetite, thirst, impaired taste, pasty tongue, tenderness in the epigastrium, and constipation. Nausea and vomiting sometimes usher in the attack, and in some cases vomiting continues for several days. In the so-called abdominal form of influenza these symptoms are more severe, and diarrhœa frequently constitutes an urgent symptom. In some of the epidemics the intestinal catarrh has shown a tendency to run into dysentery.

The countenance expresses anxiety and depression. There is pallor, together with injection of the conjunctivæ, puffiness of the eyelids, and redness of the tissues of the nostril. The facies is sometimes slightly flushed and may suggest that of enteric fever.

Catarrh.—A more or less extensive hyperæmia of the mucous membrane of the respiratory tract is invariably present, and may be said to be characteristic of the disease. There is coryza, often severe. The eyelids may be swollen and reddened; there is lachrymation; sneezing is frequent, and in many cases there is an abundant discharge from the nostrils. Epistaxis is not rare. Erythematous angina, with tickling sensations and difficulty of swallowing, is frequent. In many cases the catarrhal symptoms are restricted to the upper air-passages. Implication of the larynx is shown by huskiness or loss of voice. Hoarseness is common.

Cough is a prominent symptom. It is commonly frequent and distressing, sometimes paroxysmal from the beginning of the attack, almost always so at some period of its course. The spasmodic character of the cough in some of the older epidemics led to a confusion of diagnosis between influenza and whooping cough. The cough is apt to be worse toward evening and at night. In some cases it leads to vomiting, and by its violence and persistence gives rise to myalgia in the muscles of respiration and occasionally to hernia. It is at first dry or attended with a scanty muco-serous expectoration; later the sputa become muco-purulent, and they are sometimes streaked or mingled with blood. Toward the close of the attack the cough becomes less urgent and loses its spasmodic character. In some of the epidemics cough has not been a prominent symptom, and cases may be encountered in most epidemics in which well developed influenza runs its course with little or no cough. Various râles may be detected during the course of the attack as in ordinary acute bronchitis. In other cases râles are absent and the auscultatory signs are negative.

Dyspnœa is not infrequent. It may occur in cases where none of the objective signs of any pulmonary lesion can be discovered. In this case it may be of nervous origin, and a direct disturbance of the function of the vagus has been invoked in explanation of it. This view is rendered plausible by the fact that the dyspnœa is occasionally intermittent and paroxysmal. In some of the epidemics orthopnœa and suffocative attacks have been common. Stitches in the side and substernal pain occur without appreciable physical signs. Hæmoptysis may occur in patients who present no physical signs of lung disease.

Nervous System.—Marked lowering of muscular strength is a very early symptom and constitutes one of the most remarkable features of the disease. Patients are extremely weak from the onset of the attack and exhausted by slight bodily effort. The ordinary strength is not regained until convalescence is far advanced.

Headache is a constant symptom. In addition to the general headache which marks the onset of the specific fevers, severe pain across the brows and in the orbits is scarcely ever absent. These pains are referred to the region of the frontal sinuses and nasal ducts, sometimes to the region of the antrum of Highmore or to the Eustachian tube and the middle ear. They are often most intense. They last commonly until the end of the attack, and in many cases persist as sequels. The head pains increase in severity toward evening. In some instances the occurrence of epistaxis has afforded temporary relief. The headache may be limited to one orbit, one side of the forehead, or one side of the face. Neuralgia in the distribution of the branches of the fifth pair is not infrequent. Hyperæsthesia of the surface of the head and neck and painful stiffness of the muscles of the neck are encountered. Among the more constant symptoms of influenza are the very severe pains in the back and limbs already referred to. There are sensations of soreness and bruising, such as follow severe and unaccustomed muscular effort; dull tearing and burning pains may be felt in particular muscles or tendons, and are very common in the calves of the legs. These pains are neither relieved nor aggravated by gentle movement or by moderate pressure.

Restlessness, insomnia, and anxiety occur in most of the severe attacks. Dizziness and faintness are not uncommon. Mild delirium is frequent; the more intense forms of delirium are occasionally observed. Somnolent states may also occur. Hebetude and torpor have characterized some epidemics. In grave cases painful cramps, subsultus tendinum, twitchings, and trembling of the hands occur. The mental power is enfeebled.

Special Senses.—The acuteness of the special senses is diminished. The sense of smell is frequently entirely lost, and that of taste greatly impaired. Many patients complain of a disagreeable coppery or metallic taste. The hearing is somewhat blunted. Severe earache is not uncommon. Suppuration of the middle ear and perforation of the membrane occur in a considerable proportion of the cases.

COMPLICATIONS AND SEQUELÆ.—The most important complications are those connected with the respiratory tract. The hyperæmia and bronchitis which occur in the severer cases cannot be properly looked upon as complications. In many instances, however, the bronchitis becomes intense, implicating the large and small tubes and giving rise to a prolonged symptomatic fever, which may even be accompanied by delirium. Broncho-pneumonia is not infrequent in children and aged persons, and may lead to a fatal result from progressive restriction of the respiratory surface or cardiac failure. This complication develops insidiously usually about the fourth or fifth day, but it may set in as early as the second day, or later during convalescence. The symptoms are frequently at first obscure, and extensive involvement of the lung may take place without great rise of temperature. Croupous pneumonia is less common. It is a late complication, occurring toward the close of the attack or when the patient is beginning to get about. It presents the usual physical signs of pneumonia, and does not commonly differ in other respects from croupous pneumonia of the ordinary form. Both lungs are frequently involved. The crisis may occur late or defervescence may take place by lysis. In some cases, however, the pneumonia occurring after grippe is afebrile. Great feebleness of respiration and a tendency to cardiac asthenia characterize this form of pneumonia. Low muttering is apt to occur, and there is frequently jaundice with slight intestinal hemorrhage. Abscess or gangrene of the lung may follow the pneumonia of grippe.

Pleurisy is not an uncommon complication, and empyema may occur. Purulent pericarditis may occur in connection with pneumonia or independently of that complication. In aged persons serous effusion into the pleural sacs is now and then encountered.

Parotitis is a rare complication of influenza.

The infecting principle of grippe exerts a powerful depressing influence upon the heart, both during and after the attack. The nutrition of the cardiac muscle is impaired and its innervation is deranged and enfeebled. Cardiac asthenia, often of a high grade, results. I have not personally seen either endo- or pericarditis occur. The murmurs which I have noted have been endocardial and either dynamic or hæmic.

Among the complications relating to the nervous system cerebro-spinal meningitis is to be mentioned. It is fortunately of comparatively rare occurrence. The cases may run an acute course like that of epidemic cerebro-spinal fever, with intense headache, convulsions, delirium, stupor, and opisthotonos, or the symptoms may be of moderate intensity and terminate in slow recovery.

Abscess of the brain may occur as a complication. Cases have been reported by Bristowe, Sharkey, and others.

Peripheral neuritis not infrequently develops during the course of the attack.

General asthenia constitutes the chief and most constant sequel. The profound nutritive derangements of the acute process are at once followed by manifestations of [illegible] of varying grade and duration.

It is, however, often extreme—altogether out of proportion to the intensity of the symptoms and their duration—and frequently lasts for weeks or months. It is important in this connection to note that this post-influenzal asthenia bears no constant relation to the original severity of the case, many apparently light attacks being followed by profound and prolonged loss of strength, while cases of great intensity often terminate in comparatively early and complete recovery. Nor is this difference in many instances merely accidental. The manifest explanation is to be found in the fact that in severe cases the patients are obliged to keep the bed and receive perforce necessary care during the active period of the attack, while those whose symptoms are slight remain up and are neglected.

I. SEQUELÆ RELATING TO THE RESPIRATORY TRACT.—1. *Bronchitis.*—It is not to be wondered at that an acute affection characterized by active catarrhal processes affecting the mucous membrane of the respiratory tract should, in a considerable proportion of the cases, be followed by a lasting and troublesome bronchitis. This is the sequel that more than all others attracted the attention of physicians in the earlier epidemics. I have noted two principal forms:

(*a*) Subacute bronchitis, with little constitutional disturbance, but marked physical signs, and an abundant tenacious, muco-purulent expectoration. This condition lasts for several weeks and terminates in complete recovery.

(*b*) A bronchitis which resists ordinary treatment, and, with varying ameliorations and exacerbations, gradually establishes itself as chronic. In other words, the attack of influenza proves the starting-point of a bronchitis which is chronic from the outset.

2. *Broncho-pneumonia* has been observed in a large proportion of the cases, not only as a complication, but also as a sequel—a fact for which the catarrhal inflammation of the respiratory mucous membrane and the acute prostration sufficiently account.

3. *Croupous Pneumonia.*—All practitioners have been impressed with the frequency with which croupous pneumonia develops in the course of influenza or during convalescence. The association of these two diseases has much to do with the high death rate of influenza in certain epidemics—more, perhaps, than has generally been ascribed to it, for the reason that the symptoms of influenza may, in cases of unusual severity, mask those of the intercurrent affection. Nor is it remarkable that pneumonia, so often intercurrent in acute diseases, should arise as a complication. Occurring as a sequel of influenza, pneumonia frequently involves the upper lobe—apex pneumonia. It occasionally runs a very protracted course, and under these circumstances often assumes the guise of tuberculosis—pneumonic phthisis or phthisis florida. I have encountered several cases in which the differential diagnosis presented great difficulty, was rendered hopeful only by the absence of tubercle bacilli from the sputum, and finally confirmed by recovery. In these cases high and irregular temperature, continuing for several weeks, with copious muco-purulent expectoration, rapid wasting, sweating, apex dulness, with diffuse subcrepitant râles, especially when there is a marked family predisposition to pulmonary tuberculosis, render the clinical picture alarmingly like that of a galloping consump-

tion. All the cases of this nature that I have seen terminated in complete recovery.

4. *Pulmonary Consumption.*—Far more numerous, however, have been the cases in which influenza has been the point of departure for actual pulmonary consumption. The patients have been persons in whom the hereditary predisposition was marked or who were living under conditions, such as association with consumptives, which singularly exposed them to infection. Under these circumstances the symptoms of influenza have passed away, leaving, usually, merely debility with slight cough and expectoration, such as attend an ordinary bronchitis. But these symptoms have persisted, not yielding to treatment, and after a time, upon examination, tubercle bacilli and localized dulness have been found.

5. *Pleurisy.*—Whether or not the infecting principle of influenza directly causes pleurisy cannot in the present state of knowledge be positively affirmed. Plastic pleurisy constantly, pleurisy with effusion occasionally, arise in connection with croupous pneumonia and tuberculosis occurring as sequels of influenza. The stitch in the side of influenza is probably in most cases pleurodynia, as it is unaccompanied by friction sounds and as a rule quickly passes away. Intercostal neuralgia is not rare, even with herpes zoster, in the course of or as a sequel of influenza, and may sometimes mislead; but it is certain that secondary infections, to which the lesions of the bronchial mucous membrane expose patients suffering from the grippe, sometimes toward the close of the attack, and often during convalescence, may reach the pleura and give rise to inflammation of that structure. The pleurisy arising under these circumstances may be plastic or it may be accompanied by serous or purulent effusion, and does not differ from that caused by similar infections under ordinary circumstances. To this general statement there must, however, be noted an exception. In a number of instances in persons previously in good health I have seen influenza followed by pleurisy of an unusual form. The symptoms have been acute and very severe. Among them the following were especially marked: Great pain, limited to the region of the apex, irregular high temperature, often reaching 104–105° F., coarse, rubbing friction sounds, slowly increasing dulness, with feeble distant breath sound, no bronchial respiration; cough has been slight or absent, and there has been little or no expectoration; constitutional disturbance has been great; the physical signs at the base and upon the opposite side have been without significance. These phenomena have warranted the diagnosis of a rapidly developing apex pleurisy with great thickening—a diagnosis confirmed in my experience by a single post-mortem examination. In other instances recovery has slowly taken place with retraction, restricted movement, and permanent impairment of resonance, though the general health of the patients has remained good, and it has been impossible to find in their occasional scanty morning sputa tubercle bacilli.

6. *Asthma.*—In neurotic individuals asthma has occurred as an accompaniment of bronchitis following influenza.

7. *Otitis media* constitutes one of the more distressing complications and sequels of influenza. It is more likely to arise in cases in which nasopharyngeal lesions are prominent or persistent. The superficial

layer of the mucous membrane of the nasopharynx in the acute stage rapidly undergoes patchy necrosis, and there is an abundant irritating discharge. The ear trouble may occasionally arise without great pain, but, as a rule, the suffering is severe and tends to recur after perforation of the tympanic membrane as the thick discharge and necrotic tissue accumulate. Rapid disorganization of the structures of the middle ear sometimes occurs, with permanent deafness as a result. In many cases the suppuration yields stubbornly to treatment and persists for weeks or months.

II. SEQUELÆ RELATING TO THE CIRCULATORY SYSTEM.—1. *Cardiac Disorders.*—Hearts impaired by previous disease of the valves or wall often undergo additional damage and pre-existing symptoms are aggravated. But it is not always the damaged heart that suffers. Many of the worst cases occur in persons of previous good health. Robust, self-reliant men who scarcely know what sickness is become feeble, hypochondriacal, and valetudinarian. It has been a pitiable sight to witness the sufferings, partly physical, largely mental, of some of these patients. The actual cardiac symptoms are heart consciousness, sometimes distress, sometimes actual precordial pain, usually paroxysmal, occasionally suggestive of angina pectoris, breathlessness and faintness upon effort, unsatisfactory sleep, disturbed by dreams and startings, headache, and great languor and malaise. The physical signs are simply those of enfeebled and irregular heart action. They consist of weak impulse, faint first sound, and now and then an indistinct soft systolic murmur. The pulse is small, feeble, arhythmic, and intermittent. Much more distressing to the patient and his friends are the mental symptoms. To his general feeling of depression and disability are added tormenting fears of permanent invalidism or sudden heart failure. The condition is always distressing, sometimes alarming. Fortunately, however, experience has shown that the prognosis is favorable. These cases, even after they have lasted a year or two, quickly recover under proper treatment. In another group of cases the nutrition of the heart muscle is fairly well maintained, its innervation being chiefly affected. Here we have the intermittent heart. At regular or irregular intervals the heart drops a beat. If the patient is aware of this fact, either from feeling his own pulse or from the disagreeable precordial sensation which sometimes occurs, he is apt for a time to be much distressed by it. Presently, however, with returning health the heart dropping ceases to annoy him. In a small proportion of cases it continues to be a lasting cause of distress and valetudinarianism. Cardiac intermittence does not always yield readily to treatment, and once fully established becomes in a small proportion of the cases a permanent symptom.

Precordial pain, arhythmia, tachycardia, and bradycardia are common after influenza.

2. *Simple anæmia* may occur after grippe as after other acute diseases. It is neither constant nor intense, the brunt of the infection, save in exceptional cases, falling rather upon the nervous system than the blood. There is nothing especial in the anæmia of convalescence from influenza. It usually yields to treatment and terminates in recovery.

3. *Pernicious Anæmia.*—In four instances, however, I have seen that form of anæmia called pernicious follow grippe. One of these

cases was of peculiar interest as an illustration of the tendency of the infection to select in its attack the tissue of least resistance—the weak spot in the organism. A gentleman aged fifty nine, supposed to be in full health, had mild influenza in the spring of 1891. He kept about, but was for several days feverish and depressed. Catarrhal symptoms were slight. From this time he suddenly grew pale, and died in eighteen months, having presented all the symptoms and blood conditions of pernicious anæmia. This patient's father died at an advanced age of diabetes mellitus. His only son died at the age of thirty seven of malignant hemorrhagic measles, and a grandson, the child of the last, had benign hemorrhagic measles.

III. SEQUELÆ RELATING TO THE GASTRO-INTESTINAL TRACT.—These present little that is peculiar, and as a rule are not persistent. Occasionally a tendency to diarrhœa persists, and I have seen membranous enteritis follow the gastro-intestinal form of grippe in several instances. The suggestion that catarrhal appendicitis may arise as a late result of gastro-intestinal influenza is worthy of serious consideration.

IV. SEQUELÆ RELATING TO THE NERVOUS SYSTEM.—Headache, insomnia, and neuralgia are common sequelæ. The nervous derangements which follow grippe may consist of mere general loss of tone—neurasthenia with gastric, cardiac, or spinal symptoms predominating, or they may assume the definite aspect of substantive affections, such as hysteria or chorea; again, various motor and sensory palsies, manifestations of peripheral neuritis, may arise; finally, psychic disorders, as melancholia and the insanities of malnutrition, may occur. The nature of the nervous trouble is doubtless determined by hereditary or previously acquired predisposition on the part of the individual, and its course is not different from that of similar affections arising under other circumstances, and especially after the other acute infections, as, for example, enteric fever. The prognosis is in the main favorable. With reference to insanity following influenza, so far as I can learn its frequency has been greatly overestimated, and it is probable that persistent insanity arising as a sequel of this affection is in point of fact rare, and that it occurs chiefly, if not solely, in those already strongly predisposed to mental disorder, in whom the attack acts as an exciting cause, not specifically, but in the same way as any other powerful perturbating agent.

DIAGNOSIS.—The direct diagnosis of influenza is under ordinary circumstances unattended with difficulty. The progress of the outbreak, the number of individuals attacked nearly at the same time or in quick succession, the rapidly developing asthenia, and the prominence of the nervous symptoms serve to distinguish it from other epidemic diseases. The bacteriological diagnosis can be sometimes made by an examination of the bronchial sputum, and can be verified in doubtful cases by cultures.

The differential diagnosis between influenza and non-specific catarrhal affections attended by fever, malaise, weakness, severe headache, and pains in the limbs may be made by due regard to the causative relations of the two affections. Outbreaks of simple catarrh occur as the result of sudden changes in the weather, and are for that reason most frequent in changeable seasons, and especially at the end of winter and in the early spring. Influenza, on the other hand, is not in any way dependent upon the vicissitudes of the season, and may occur, as has been shown, indifferently at all times of the year, in wet or dry, mild or cold seasons, and in every variety of climate. No difficulty attends the differential diagnosis between influenza and ordinary sporadic catarrhal fevers, which lack the characteristic depression, neuralgic and rheumatoid pains, and the irritating cough and dyspnœa.

Some of the cases of influenza bear a strong resemblance to enteric fever in the first week. Malaise, headache, obtunded hearing, mental depression, fever, epistaxis, coated tongue, tender belly, and diarrhœa are observed in both affections. The temperature curves are, however, unlike, and the acute attack of influenza in uncomplicated cases runs its course ere the period at which splenic tumor and rose spots establish the diagnosis of enteric fever. Anders has called attention to the occurrence of influenza during the period of incubation of enteric fever. This accidental association of the two diseases may sometimes occasion difficulty in diagnosis. Cerebro-spinal fever has sometimes prevailed during epidemics of influenza. The occasional occurrence of cases of influenza with marked nervous symptoms, intense head pains, painful retraction of the muscles of the back of the neck, and vomiting, renders the differential diagnosis between these two affections extremely difficult and in some instances impossible. Whether the infecting principle of influenza is capable of directly giving rise to infection of the meninges or not remains to be determined.

Dengue, or breakbone fever, closely resembles influenza. Each of these diseases prevails in pandemics, developing suddenly, advancing rapidly, affecting almost all the inhabitants of regions invaded. They resemble each other in the frequency of relapses and the liability to repeated attacks during the same outbreak; in the fact that they are not self-protective; in the want of accord between the gravity of the symptoms and the low death rate of uncomplicated cases; in the suddenness of the attack, intensity of the pains, and high degree of mental and physical depression. Influenza lacks, however, the cutaneous manifestations, the remission in the course of the fever, and the tendency to arthritis which are seen in dengue. It differs from dengue also in the liability to serious complications and in prevailing in all climates.

PROGNOSIS AND MORTALITY.—Death scarcely ever occurs in uncomplicated cases except at the extremes of life. The very young bear influenza badly; the aged bear it worse still. Pre-existing disease often modifies the course of influenza unfavorably. Individuals suffering from chronic bronchitis, emphysema, fatty heart, and nephritis offer poor resistance to the depression of grippe. Phthisis and other exhausting diseases increase the danger of the attack. Cases attended by very severe symptoms usually recover, unless the patients be very young or very old or the subjects of some complicating malady. The prognosis in individual cases is greatly modified by the character of the prevailing epidemic. In some of the epidemics the death rate has been low and the mortality from other diseases not greatly increased. More commonly the death rate of endemic affections is much increased, and in some of the older epidemics influenza appears to have been attended by a high direct death rate.

The deaths from influenza reported in Paris, December, 1889, and January, 1890, numbered only 213, while the general mortality exceeded the average by 5500.

TREATMENT.—*Prophylaxis.*—Effective preventive measures are as yet unknown. Unfavorable sanitary conditions, overcrowding, damp unhealthy dwellings appear to increase the prevalence and severity of the disease; the opposite conditions of living do not, however, secure immunity. During an epidemic the aged, those enfeebled by chronic diseases, those subject to bronchitis, consumption, emphysema, degenerative disease of the muscles of the heart, and nephritis, should be cared for with solicitude, since they constitute the class especially prone to the graver complications of the disease and contribute a large contingent of the fatal cases. During an epidemic the isolation of a patient who has developed the symptoms of the disease, either in his home or in a hospital or other public institution, does not secure, as in certain of the other contagious diseases, protection for those about him—a fact to be explained by the activity of the infecting principle and the intense susceptibility of individuals in all classes of society. The segregation of the patients and their attendants and the disinfection of the belongings of the patient and the apartments are not necessary. The nasal and bronchial discharges should, however, be disinfected. Every case, however mild, should be regarded as likely to be serious, and the patient should be confined to the bed or to the couch for some days.

Prophylaxis against the attack is theoretical and to a great extent impracticable; prophylaxis against sequels is in the highest degree practical and useful.

The Management of Cases.—The treatment of influenza is expectant and supporting. Not only are epidemics self-limited, tending to rapidly exhaust the susceptibility of a community, but the individual attack is also of definite duration and self-limited, tending to run its course in from three to four or at most, in the absence of complications, in from seven to ten, days. Where the duration of the attack is prolonged beyond the period indicated, complications are almost invariably present. In all epidemics the majority of the cases are of mild intensity. The management of this group of cases should be for the most part hygienic. Patients are uncomfortable and anxious, easily fatigued, and unfitted for their usual avocations. It is only exceptionally that they consult the physician. It is unfortunate, however, that this is the case, since those who continue their avocations and duties and expose themselves to unfavorable influences during the attack not infrequently manifest at a later period the most serious results of the disease. In point of fact, the patient should even in the milder cases abandon for the time being his ordinary avocation. He should remain within doors, preferably upon a couch, for at least two days, and only gradually resume his accustomed duties.

The diet should be restricted to the ordinary fever foods. Milk is especially indicated, and may be given in doses of from one litre to a litre and a half during twenty-four hours in divided doses. Egg albumen stirred into water, flavored with a little brandy or wine, or eggnog, milk punch, or gruel, may occasionally with advantage replace the ordinary allowance of milk. Hot beef tea or concentrated meat extracts are to be avoided. They very frequently increase the headache and languor. Cold drinks in moderate quantity are usually acceptable to the patients. Weak wine whey, a mixture of equal parts of seltzer water and milk iced, koumyss, matzoon, and similar preparations, enable the nurse to furnish the necessary changes where the stomach is irritable.

The administration of alcoholic stimulants must be regulated in part according to the previous habits of the patient, in part according to his immediate condition. Abstemious persons may not need them, but those who have been in the habit of taking alcohol, the aged, and those debilitated from previous sickness are benefited by the judicious use of alcoholic beverages.

Early in the course of the attack a laxative may be necessary. This may consist of some form of saline or a laxative dose of calomel, or the latter administered at night, followed by the former in the morning. Caution is, however, necessary in the use of purgatives in influenza, since in a very considerable proportion of the cases gastro-intestinal symptoms with diarrhœa occur, and in some instances are difficult of control.

The analgesic antipyretics are to be used cautiously in view of the tendency to general, and especially to cardiac, asthenia. Nevertheless, the guarded administration of antipyrin, phenacetin, migranin, and other members of this drug group are often necessary to relieve the agonizing pain of influenza. Small doses of phenacetin and sodium salicylate, administered in powder or capsule at short intervals, very often exert a powerful influence in mitigating the sufferings of the patient. Small doses of Dover's powder repeated at intervals of two or three hours are likewise of benefit. I cannot say that I have seen any advantage from the use of warm baths, foot baths, or diaphoretic drinks, the patients usually preferring to remain undisturbed. Advantage sometimes follows the administration of small doses of morphine, with which, in the case of extreme sweating, minute quantities of atropin may be added. If there be great restlessness and jactitation, the hypodermic injection of morphine, together with hyoscin hydrobromate, proves useful. Quinine in small doses is without effect. In large doses it simply augments the sufferings of the patient. There is no adequate evidence to show that quinine in any dose favorably modifies the course of the attack or aborts its duration. During convalescence iron and bark, and in particular strychnine in full doses, are to be administered.

In the milder cases the catarrhal symptoms call for no special measures of treatment. When intense the coryza, tonsillitis, laryngitis, and bronchitis are to be treated upon general therapeutic plans. Inunctions of fatty substances about the brow and over the bridge of the nose are sometimes useful in relieving the distress of the coryza. Animal fats, such as washed lard, cold cream, and the like, are preferable to the mineral fats—cosmoline and vaseline. A 2 per cent. solution of morphine and cherry-laurel water may be snuffed into the nostrils. The pains associated with the coryza and the neuralgic pains are to some extent mitigated by a flannel nightcap or silk handkerchief tied about the head. Tickling cough may be relieved by steam inhalations and the application of sinapisms over the manubrium. In the graver cases prominent indications for treatment are to be found in the fever, the catarrhal process, the asthenia, and the pain and sleeplessness. It is especially important that the failure of the powers of the circulation which are characteristic of the disease should be anticipated by efficient supporting treatment. This is particularly urgent in the case of influenza affecting infants, the very old, and those previously debilitated from any cause.

The febrile movement is not usually excessive, almost always transient. A fever regimen should be adopted. The disinclination to take food is often so great that a sufficient quantity can scarcely be administered, especially in the early days of the attack. Small amounts of nourishment must be given at regular hours. As convalescence begins patients should be urged to take food. The quantity taken at one time should be increased and the intervals between feedings prolonged. At least enough fluid should be taken to assuage thirst. The ingestion of simple beverages exerts a favorable action upon the skin and kidneys. The frequency of spontaneous sweating and the readiness with which free perspiration may be induced must be looked upon as a contraindication to the use of diaphoretic drugs.

General and local bloodletting, emetics, nauseants, and drastic purgatives are to be avoided in the treatment of influenza.

For the relief of the distressing cough no drugs are more effectual than opium and its derivatives, especially morphine and codeine. It is important to observe the same caution in administering this group of medicines to infants and aged persons in influenza that is necessary under other circumstances. The influence of carbolic acid in restraining cough makes it a useful adjuvant. The bromides, paraldehyde, chloralamide, trional, and chloral may be used for the relief of jactitation and insomnia. Chloral should be used with great caution. Gastro-intestinal symptoms must be managed in accordance with general principles. If of moderate intensity, they require no special treatment. Complications are to be treated in accordance with general therapeutic indications, especial attention being directed to the asthenia which is so prominent and disastrous a tendency in grippe.

The treatment of influenza demands the most careful attention of the physician, who must be on guard to detect the inflammatory lung complications, which so often lead up to a fatal issue, as early as possible. The circumstances of the individual case, the age of the patient, the nature of the complications, and the effect of remedies must be carefully taken into account. All measures that tend to depress the general nervous system, the functional activity of the respiration, or the heart power are to be carefully avoided.

During the convalescence the patient should be treated with equal, even more, care than those convalescing from other acute infectious diseases. Rest in bed, a systematic diet of high nutritive value, strychnine, iron, and later change of climate, are important. The patient should be instructed as to the liability of pulmonary disorders, which may become

regard to the necessity of limiting for a time the appli-
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EPIDEMIC CEREBRO-SPINAL MENINGITIS.

BY THOMAS S. LATIMER, M. D.

SYNONYMS.—Cerebro-spinal fever; Spotted fever; Lepto-meningitis.

DEFINITION.—A specific infectious disease of microbic origin, but little if at all contagious, characterized by inflammation of the lepto-meninges, with disturbance of function of the whole cerebro-spinal axis, motorial, sensory, and psychical, with strong tendency to a speedily fatal issue.

HISTORY.—Epidemic cerebro-spinal meningitis has been known from the earliest years of the present century, but was first accurately described by Viesseux in Geneva in 1805. It appeared in the United States in 1806, and continued with but little interruption for ten years. During this time it also made its appearance in Spain, Germany, Italy, Algeria, and Denmark. In 1854 it broke out in Sweden with severity, causing 4000 deaths. Slight epidemics occurred in Germany in 1822, but it was not until 1863 that it was there of frequent occurrence. v. Ziemssen, writing in 1874, says that it had then become domesticated in Germany. Since then Strümpell says there have been more or less extensive epidemics every year. It broke out in the workhouses of Ireland in 1846, and appeared in severe form in Dublin in 1866–68. In Fagge's *Practice of Medicine*, published in 1886, it is stated that Scotland and England had been almost exempt up to that time. It was first observed in this country at Medfield, Mass., in 1806. After this scattered epidemics of moderate severity appeared in various parts of the United States up to 1816, when the disease disappeared, to recur in Middletown, Conn., in 1822–23. Since then it has been of frequent recurrence in various parts of the country. At Carbondale, Pa., 400 persons died from this cause out of a population of 6000. In Pepper's *American Text-book*,[1] a tabulated statement, begun by Stillé in 1863 and carried on to 1883, and completed by Pepper up to 1892, shows that it prevailed continuously during this period in Philadelphia; the smallest mortality for any one year was 23 in the year 1891. The total mortality reported in this city for this period was 2575. Numerous cases occurred in both armies in the late American war, but it cannot be said to have had any widespread prevalence in either.

ETIOLOGY.—The essential cause of epidemic cerebro-spinal meningitis is not yet definitely determined, though a large body of evidence tends to establish such a relation with the *micrococcus lanceolatus encapsulatus*. This organism is found almost invariably in the exudates, meningeal and cerebral, and in the lungs in cases complicated with pneumonia. Eberth first isolated it in 1880 in a case of meningitis secondary to pneumonia; Bozzolo and Leyden in 1883; Weischelbaum in 1886; Netter in the same year; Goldschmidt in 1887; Ortman, Foa, and Bordoni-Uffreduzzi in 1888; Banti in 1889; and Bonome in 1890. Mirto obtained it from the exudates in 1891, and inoculated rabbits with it, producing septicæmia. Klippel in 1891 and Ribbert in 1892 found it in sporadic cases. In Welch's laboratory in Baltimore in 3 recent cases the same organism was found (Flexner and Barker).

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[1] *An American Text-book of the Theory and Practice of Medicine*, Pepper, vol. i. p. 163.

Other organisms, however, have been frequently found associated with cerebro-spinal meningitis; thus, according to Flexner and Barker, in 1889 Netter found the Friedländer bacillus in a case of meningitis following otitis media. Mills, in a case of pneumonia associated with meningitis, thought he had discovered the same organism. Monti in a case of pleuritis with arthritis obtained the *micrococcus lanceolatus* in 1889. Adenot in the same year and Kainen in 1890 each isolated a bacillus which they supposed to be the typhoid bacillus. Debove, in a case associated with peritonitis, obtained a pneumococcus. Hanot and Luzet isolated streptococci from the exudate from the meninges in a case of general infection resulting from puerperal fever. The *staphylococcus pyogenes aureus* was found in a case associated with otitis, broncho-pneumonia, and arthritis by Le Gendre and Beaussenat in 1892. Klippel in 1892, in a demented individual who died of acute meningitis, observed the *micrococcus lanceolatus* over an area of brain softening where the exudate was most abundant.

Boulay and Courtois-Suffit in 1890 isolated the *micrococcus lanceolatus* from a case of combined meningitis and peritonitis without pneumonia; and Bonome found the same organism—pneumococcus—in a case of combined pericarditis and meningitis. Zorkendorfer, from Chiari's laboratory, reports a case of purulent meningitis associated with inflammation of the ethmoidal cavity and suppuration in the sphenoidal sinuses, in which diplococci were found in the pus taken from the sinuses and from the meninges. Pure cultures of these caused fatal septicæmia in rabbits, in whose blood organisms were found not distinguishable from the *micrococcus lanceolatus*. Drs. Flexner and Barker—to whom I am indebted for most of the historical facts here mentioned—found the micrococcus lanceolatus in a case of traumatic meningitis with no other focus of infection. Prudden likewise isolated it in a case of traumatic meningitis, a patient of Holt's.

Streptococci and staphylococci have also been found by various observers, and by Roux a bacillus resembling that of typhoid fever; by Mircoli, the *bacillus pyogenes fœtidus*. Netter clearly traced meningitis to the pneumococcus in 16 out of 30 cases in which no pneumonia had existed. The number of cases examined is as yet too small to warrant the statement that the *pneumococcus lanceolatus* is the single and only cause, but the facts recited above go far to show that, although other organisms are often found and the pneumococcus has not invariably been shown to be present, it is, however, so much more frequently present than any other pathogenic microbe that it may fairly be considered the causative agent in a large proportion of cases.

If, however, it is admitted that this organism is the specific cause of epidemic cerebro-spinal meningitis, the frequency with which it is found in sporadic and traumatic cases makes it impossible to distinguish the epidemic from other forms of meningitis. It is generally admitted that the clinical phenomena are not widely dissimilar in the various forms of meningitis, and if this etiological factor is not peculiar to the epidemic form, then all meningeal inflammations are essentially the same, and any traumatic or sporadic case may be a point of departure in epidemics of this disease.

The frequency with which the *micrococcus lanceolatus* is found in the mouths of healthy individuals (80 per cent., Netter) would indicate that under certain conditions—antacid or hypoacid states of the gastric secretion or other unknown conditions—it may pass through the stomach into the circulation, and, acquiring a virulence not before possessed, give rise to meningeal and other inflammations, thus becoming truly auto-infective. Such an origin of course does away with the necessity for contagion or the introduction of the microbe with food or drink. It is almost uniformly present in health, and requires only some alteration in the condition of the host to invest it with virulence. If so, we must seek an explanation of its epidemic prevalence in the environment of the individual. The atmospheric conditions, character of the water and food supply, season, shelter, clothing, occupation, and any of the many conditions affecting the general health, are without special bias until the entrance of a specific organism or a newly acquired virulence gives it. Of these predisposing causes—predisposing to epidemic prevalence—we have comparatively little definite or positive information. It may be said in general terms that extreme cold of long continuance; bad food, especially if in process of decomposition; drinking water containing abundant organic impurities; breathing the foul air of crowded tenement-houses; insufficient and uncleanly clothing,—may all be conditions so impairing the vigor of the individual, while favoring the multiplication of the organisms and determining greater virulence, as to cause epidemic outbreaks where otherwise a sporadic case or two only would be found. These conclusions, however, which seem reasonable enough, cannot readily be sustained by any positive evidence at our disposal.

In the winter and spring of 1893 an extensive epidemic of cerebrospinal meningitis prevailed in the vicinity of Lonaconing, a mountain village of about 5000 inhabitants in the coal-mining region of Maryland, which was carefully studied by Drs. Simon Flexner and Lewellyn F. Barker of the Johns Hopkins University staff in the Department of Pathology. The well-known ability of these gentlemen and the painstaking manner in which this study was conducted, make their report one of the most (if not the most) valuable recent contributions to the study of this disease. It will be understood in what follows that whenever reference is made to the Lonaconing epidemic it is done on the authority of their report and that of R. L. Randolph, assistant ophthalmic and aural surgeon of the Johns Hopkins Hospital, whose report is limited to the ophthalmological phenomena observed in this epidemic.

The village of Lonaconing is situated in a deep gulch in the Allegheny Mountains, through which a muddy creek of considerable size runs. All the streams in this vicinity are subject to speedy rise after a heavy rainfall of even brief duration. The houses are situated in terraces on the side of the valley and mountain through which the stream runs. Tier above tier rise on the side of the mountain the houses occupied by the miners, while in the valley are situated the business and professional houses. Above the level of the dwellings are placed the privies, which must constantly pollute the soil about them, and after rainfall, as indeed at all times, foul the stream running through the town. The stables are quite close to the dwellings. On the arrival of Drs. Flexner and Barker the snow which had recently fallen had already begun to melt with the effect thus described:

"The water streamed down the mountain sides, carrying with it the general refuse from the yards, the material from the cow stables, and the excreta from the outhouses of the upper tiers, through the yards, past the dwellings situated below, and finally entering the creek, which acts as a huge sewer winding through the centre of the town. On their way these polluted surface washings found no system of drains for their reception, and in places crossed the common roadway in little rivulets, through which the inhabitants of the town had to drive and walk."

The water supply of the village is obtained from surface wells and from cisterns, and in many instances the surface water with its accompanying filth was seen flowing directly into these wells, which are in constant use for drinking water. They may be further supposed to be contaminated by filtration of water from the creek, which is itself additionally fouled by slaughter-houses built on its margin, from which the blood and other noxious matters find ready entrance into its waters. In many instances the houses of the miners are overcrowded; in one house in which was a fatal case eleven persons slept in three bedrooms. The houses were generally very close together. Many, however, were commodious, well built, and not overcrowded; these possessed no immunity, and the majority of cases prevailed in the higher rows. One fatal case occurred in an isolated dwelling on a high hill a quarter of a mile distant from any other dwelling. A number of cases, however, occurred in the lower sections, and there were numerous sporadic cases more or less distant from the site of general prevalence.

The earliest cases were in two young men, aged respectively twenty-one and twenty-two years, who in January, 1893, after a dance in which they were overheated, exposed themselves to extreme cold, so that "their hair, wet with perspiration, was frozen upon their heads." A long and cold drive to their homes followed, and on the next day they were attacked with cerebro-spinal meningitis. Immediately afterward the disease became epidemic at many different points in the same region, and prevailed continuously during the succeeding months up to the middle of May. Fresh cases occurred with every decided diminution of temperature; and by the 1st of March 68 well marked cases and 40 classed as abortive had been recorded. No notable difference attributable to sex was observed, and though, as usual, children were most often attacked, it was by no means limited to them.

An outbreak in the neighboring town of Frostburg ran the total number up to 200.

In this epidemic it is noteworthy that such a condition existed as is favorable to the development and spread of infectious diseases in general, and that there was an actual prevalence at the same time of scarlatina, diphtheria, and other diseases of this class. It is also shown how close is the relation to season, and even to variations of temperature in the same season—a fact frequently observed before.

That external variations in temperature should so decidedly influence the epidemic prevalence of this disease is somewhat remarkable, as it is of course attended with little or no alteration in the temperature of the medium in which the organism lives. It cannot therefore materially affect its life history, apparently tending rather to produce such unknown conditions in the host as favor the development of meningeal inflammation without obvious increase in numbers or virulence of the parasite.

According to J. Lewis Smith,[1] statistics collected in Europe and America show that 166 epidemics occurred "in the six months commencing with December; only 50 were in the remaining six months of the year." Hirsch, who found 57 epidemics occurring in winter and but 20 in other seasons, thinks this tendency is rather a result of the crowding and bad ventilation incident to cold weather than to the direct effect of cold. The moist atmosphere probably present from the melting of snow and overflow of streams furnishes a favorable condition heretofore observed especially by Wollf, who in a series of 132 cases treated in Hamburg in hospital came to the conclusion that atmospheric moisture was a strong predisposing influence. That fatigue associated with exposure may be a potent predisposing influence is shown, not only in the two cases that first occurred in the Lonaconing epidemic, but in numerous other instances, notably in the brigade of General Butterfield of the U. S. Army during the late war, where, according to Frothingham, it seemed to be connected with exhausting drilling; and also in the epidemic of 1811 in Vermont, where the outbreak in the command of General Dearborn, which was fatigued by exhausting marches and dispirited by defeat, was of especial severity.

The filthy condition of the drinking and cooking water at Lonaconing would favor the idea that here the state of the water supply sustained close causal relation to this disease; but the force of this conclusion is impaired by the fact that the occupants of the upper tiers of houses suffered most.

That a crowded condition of many of the houses in this locality favored the diffusion and fatality of this epidemic is extremely probable, as a like tendency has frequently been observed in crowded tenement-houses, barracks, and prisons; but it has frequently prevailed extensively in cleanly villages where there was no crowding; and it will be remembered that in the commodious and well built houses in Lonaconing the occupants were not exempt.

That this disease is directly communicable from person to person is unlikely under ordinary circumstances. Attendants are not much, if at all, more liable to contract it than others in the same community, but a sufficient number of cases, apparently traceable to personal contact with the infected or with clothing, warn us that this mode of origin is at least possible. Hirsch, J. Lewis Smith, Kohlman, and many others have reported cases that admit of no other reasonable explanation; therefore the unaffected should receive the benefit of the doubt and all unnecessary intercourse with the affected should be forbidden. On the other hand, no unnecessary alarm need be felt because of unavoidable association with the contaminated, since the closest intimacy has often failed to transmit the disease. In an epidemic of 30 cases occurring in

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[1] J. Lewis Smith, *Diseases of Children*, p. 363.

Cologne no two cases were in the same house. Radzowski reports a case in which a woman through a three weeks' illness suckled her babe without infecting the child. Immunity is not acquired by one attack. Gowers relates a case in which a woman died in one epidemic who had recovered from a similar attack five years before.

A very common circumstance is the association of epidemic meningitis with other acute diseases; this is especially the case with croupous pneumonia. In Erlangen between 1866 and 1872 no less than 14 instances of such association were recorded (Fagge). That this is a fact of especial significance as bearing on the etiology of the disease is quite clear when we reflect that the *pneumococcus lanceolatus* is the microbe common to both diseases. It is nevertheless true that other organisms are found with sufficient frequency to compel the admission that meningeal inflammations, including the epidemic form, may be excited by other microbes, and to give some warrant to the nomenclature at present not uncommonly used. Grasset, for example, speaks of a meningeal pneumococcus, *pneumococcus meningitis*, of which he recognizes two varieties—one occurring by extension from inflamed mucous membrane in the ear, nose, or pharynx, where the organism is harmless in health, or it may supervene in general infection arising at some distant point. Writers also speak of a *streptococcus meningitis*, a *typhoid bacillus meningitis*, a Klebs-Löffler *bacillus meningitis*, a golden *staphylococcus meningitis*, and an *influenza meningitis*.[1] It would greatly simplify matters if the facts warranted the statement that epidemic meningitis was peculiar in its etiology and arose only from pneumococcus infection, even though we had to admit some peculiar state of the body or of the microbe at the time of epidemic prevalence to account for this circumstance, while other forms of meningitis had varied modes of origin. We must, however, reluctantly admit that this conclusion is not justified in the present state of our knowledge.

Possibly the explanation may be found in the manner in which other microbes or their toxins may be associated with the pneumococcus, as in the suggestive observations of E. Mosny related in *La Semaine médicale*, January 4, 1895. This observer instituted a series of experiments in Straus's laboratory in order to determine the influence on the pneumococcus of various microbes with which it is usually associated in cases of pneumonia in man—viz. the *staphylococcus pyogenes aureus*, Friedländer's *pneumobacillus*, and the *streptococcus pyogenes*. His results, so far as the *staphylococcus pyogenes aureus* was concerned, were that in every case association of living cultures of the *staphylococcus aureus* with living cultures of the pneumococcus increased the virulence of the latter microbe, and this was especially marked when both cultures were inoculated simultaneously at points distant from each other under the skin of both thighs. Rabbits thus inoculated died within a day, while the control animals lived a fortnight. Simultaneous inoculation in the blood of the two cultures at the same point caused death within three days; the control animals died in five days; similar inoculation under the skin killed a rabbit in four days; while in inoculation with the pneumococcus alone the control animal did not die for a fortnight. Even twenty four hours after inoculating with the pneumococcus, inoculation with living cultures of the staphylococcus increased the virulence of the former, though to a less degree. In all these experiments the pneumococcus was found in a state of purity in the blood of the heart and at the point of inoculation when this was in the skin, while the staphylococcus was found only in the kidney and at the point of inoculation, never in the blood. All this points to the conclusion that the virulence of pneumococcus is increased by association with the staphylococcus or its toxins.

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[1] *Journal of Nervous and Mental Diseases*, Jan., 1895.

It would be interesting to know the exact manner of death in these animals, and to what extent, if at all, meningeal inflammation existed. With the pneumococcus in a state of purity in the blood of the heart, with added virulence derived from the staphylococcus, we would naturally expect such a result, unless we must also have, to attain this end, a diminished resistance on the part of the meninges—what Jaccoud calls the "morbid opportunity." Otherwise we are entitled to a little skepticism as to the potency of this microbe as an excitant of meningitis.

In the Academy of Medicine, Paris, May 7, 1895, Cornil related a case of suppurative meningitis distinctly influenzal, as none of the ordinary pus-producing microbes were present. In this form of meningitis the pus is, according to Cornil, serous and less opaque than in the pneumococcus or streptococcus meningitis.

The following conclusions seem fairly warrantable from the facts above narrated:

1st. Meningeal inflammation, cerebral or spinal, is due to the presence of pathogenic germs. The same organism is sometimes found in sporadic and in epidemic cases; any sporadic case may therefore be a centre of endemic or epidemic prevalence.

2d. The organism most frequently associated with it is the *pneumococcus lanceolatus*.

3d. Various other organisms—streptococci, staphylococci, and bacilli—are present sufficiently often to justify the belief that they may also be excitants of this disease.

4th. The epidemic prevalence of cerebro-spinal meningitis is probably due to the influence of external conditions on the individuals affected, rendering them more susceptible to the pathogenic action of the infecting microbe.

5th. The best known of these external influences are cold, moisture, fatigue, crowding, and foul water, yet it may occur in the absence of any of these predisposing causes; hence it may be inferred that changed conditions in the host may develop especial virulence in the parasite, yet this cannot affect the propagation of the disease unless it is assumed that the virulent microbe is transmissible when under ordinary circumstances it is not. On the whole, it seems more reasonable to conclude that the host becomes more susceptible, more liable to meningeal inflammation, than that the parasite becomes more virulent; there is a diminished resistance rather than an added force.

The mode of access of the microbe to the meninges cannot be said to be positively determined, but it probably varies with many circumstances. It is almost always found in the mouth and nose of healthy individuals; hence it is not improbable that it frequently passes into the ear by the Eustachian tube, or directly into the respiratory passages, or directly through the ethmoid to the cerebral meninges, where in either locality it may or may not give rise to inflammation as the conditions are favorable or unfavorable, or as it is accompanied or not by other micro-organisms, such as streptococci or staphylococci, or as it may itself be possessed of peculiar virulence or not.

The occurrence of suppurative otitis as a condition precedent to meningeal inflammation has so often been noted as to leave little room for doubt that it furnishes a condition favorable to the development and access to the meninges of this organism. "The otitis interna, *i. e.* media, or whatever it may mean," says Goodhart, "forms a fructifying ground by which the adjacent membranes become attacked; it forms the open door by which the murderer steals in, rather than the weapon by which the injury is inflicted." A nasal catarrh or a tonsillitis may likewise furnish acceptable conditions. It is scarcely credible that an organism may be continuously present in healthy mouths and not frequently pass into the air passages to find at times conditions favorable to the development of its pathogenic properties. It is not therefore surprising that the lungs should often prove the portal to the brain, and pneumonia the primary disease to which cerebro-spinal meningitis is the legitimate successor. The pneumococcus has been found free in the blood of the heart, and so may readily pass directly to the cerebral membranes. There is a sufficient number of cases in which meningitis is the primary disease to make it extremely probable that the micrococcus may pass directly into the general circulation, and, finding other organs and tissues more resistant, effect a lodgement in the cerebral or spinal meninges, and, owing to favoring conditions but little understood, produce disturbance in them alone. Or, it may, in consequence of the effect upon the general health by the disease here established and the changes produced in the blood, render other tissues susceptible, which thus become secondarily involved. It is probable that the alimentary canal is at times the avenue by which the blood becomes affected, as the microbes must frequently be carried from the mouth into the stomach with food and drink, especially with the latter; and as simple fluids presumably do not excite an active secretion of acid gastric juice, they may escape digestion and be washed into the intestine, where the conditions are more favorable to their growth and development and to their entrance into the circulation by either lymph or bloodvessels. Flügge has called attention to this possibility in swallowing water infected with a cholera bacillus; and the experiments of Ewald, in which he found that after water was introduced into the stomach a portion passed on at once, and after a time the rest passed over suddenly without becoming acid, tend to sustain this view. Some support is also given to it by the observation of Flexner and Barker, who in the vomit obtained from one child sick of meningitis demonstrated the absence of free hydrochloric acid. One case, however, proves nothing, and of course the absence of free hydrochloric acid in a case of meningitis does not show that the stomach was free from acid before the attack: it may have been a result of the disease, and not a condition precedent, but the fact is suggestive.

Nothing is known as to the manner in which the microbe leaves the body or if it has any existence outside the body; but if it is admitted that the disease has been occasionally communicated from articles of clothing or personal contact with the sick, it follows that it is contained in some of the excreta or in the air breathed by the patient. That the micrococcus can live and retain its virulence for four months when dried in sputum or blood has been abundantly shown. "We have shown," say Flexner and Barker, "that an organism possessing the culture and morphological properties of the *micrococcus lanceolatus* is thrown off with the dejections in some cases of cerebro-spinal meningitis, and, as indicated by the experiments of Bordoni-Uffreduzzi, Guarnieri, Netter, Patella, Nikiforoff, Sirena and Alessi, and Kruse and Pansini, the organisms may retain their vitality and even virulence when dried in sputum, blood, etc., sometimes for four months." It must be admitted, however, that we have no positive knowledge of the mode of access or exit of this organism, nor of its life history outside the living body.

PATHOLOGICAL ANATOMY.—The most characteristic effects of cerebro-spinal meningitis are naturally seen in the brain and cord and their membranes. The vessels of the pia mater are engorged, the sinuses distended, and the vessel walls thickened. Effusions, serous, plastic, and purulent, occur on the surface of the convexity, at the base, and in the ventricles and central canal. On the convexity the sulci are filled with inflammatory exudates, in the later stages purulent in character. The meninges and entire cerebral surface may be bathed in pus, the membranes adherent to each other and to the cerebral surface, which may be infiltrated and softened, so that efforts to separate them are necessarily attended with cerebral laceration. The vessels of the brain are engorged and dilated and the ventricles distended. The dura of the brain is but little affected, that of the cord somewhat more.

The subarachnoid space may be filled with serum or pus, and the arachnoid meshes infiltrated, especially in the sulci. This infiltration, serous or cellular, may be sufficient to render the membrane quite opaque. It usually follows the course of the vessels, but at times occurs in scattered patches. In advanced and severe cases the membranes may be everywhere œdematous, and the cerebral substance softened to a considerable depth. Even abscesses, single or multiple, may occur. The disease is really a meningo-encephalitis and myelitis. Those cases that run a rapid course present but slight naked-eye changes beyond intense hyperæmia, but microscopic examination almost always shows extensive cellular infiltration. It is probable that a better chemical knowledge will some day demonstrate the presence of toxic agents in such quantity in foudroyant cases as to account for the rapid development of fatal symptoms. Such cases present in a striking manner the clinical symptoms of acute toxæmia. In these cases the amount of liquid effusion or of cellular infiltration is insufficient to account for the sudden development of grave symptoms and their rapid progress to a fatal issue on any hypothesis of pressure or other mechanical interference with the functions of important parts of the cerebro-spinal structure. The presence of toxins sufficiently potent to overpower the nerve centres must be assumed, and this is no very strained assumption, since their presence has been shown in so many other instances; but in this particular disease the demonstration has not been made.

The inflammation invades both convexity and base, or either alone. When the base is involved the cerebral nerves are liable to become affected and optic and aural neuritis ensues. The lymph spaces about these nerves may be filled with exudate. Structural changes in the nerve fibres are usually present in sufficient degree to account for the functional disturbances in vision and hearing so characteristic of this affection. At times this may be brought about by direct extension of the inflammatory action, with swelling of the axis cylinders of the affected fibres, sometimes issuing in their complete destruction, and attended with diminution of the white substance of Schwann; at times the transudate derived from other sources may follow the course of these nerves, and by pressure occasion degeneration; or the vessels of the nerve investments may be distended and thrombotic. Suppuration of the tympanum leading to perforation occasionally gives rise to tinnitus aurium and deafness. Inflammation of the floor of the fourth ventricle has been invoked to account for these symptoms. v. Ziemssen, however, found this condition without disturbance of auditory function.

Fagge calls attention to the curious fact that whilst the auditory nerve is frequently affected the facial nerve always escapes. This conclusion, however, is not generally accepted: Gowers says it is probable that inflammation of the membranes never damages the auditory nerve without also affecting the adjacent facial nerve. Both ears are usually affected by inflammation of the labyrinth, and deafness, consequently, is complete. In cases that recover, especially in the very young, this may result in mutism, even in those who have acquired the faculty of speech. Hirsch thinks there is at times a true aphasia immediately resulting from the cerebral affection, but v. Ziemssen failed to observe it, and I am not aware that it has been observed by others. Fagge states that in 1874 every one of the inmates of the asylum for deaf mutes at Bamburg owed the defect to an attack of epidemic meningitis.

The ventricles may be so distended with a turbid serous fluid or pus as to compress and flatten the intervening cerebral structure against the cranial vault. Very large quantities of fluid are at times present, and may indeed be said to be continuous from the meshes of the pia arachnoid through the fissures of the convolutions into the ventricles and central canal of the cord. Large serous or sero-purulent accumulations in the ventricles are commonly associated with occlusion of Majendie's foramen or of the aqueduct of Sylvius. Small hemorrhages occur in the meninges and in the substance of the brain and cord.

The cord and its membranes present appearances in all essential particulars identical with those found in the brain and its meninges. The exudates are here most abundant at the most dependent parts.

It seems, however, probable that the extent to which the posterior dorsal and lumbar regions of the cord are affected is rather because of the greater abundance of subarachnoid tissue there than because of the favoring influence of gravitation. "The disease is really one of the subarachnoid tissue, involving on the one hand the pia mater and subjacent nervous tissue, and on the other the arachnoid."[1] According to Fagge, the changes in the body of the cord are less marked than those of the brain, but this opinion finds little support in the observations of Flexner and Barker, who in the post-mortem examinations made by them found the cord lesions to be of a most marked character. In cases examined by them the pia was bathed in pus or sero-pus, its vessels injected and thickened, the membrane infiltrated, and the surface of the cord covered with exudate and its structure infiltrated with cells.

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[1] Trevelyan, *Brain*, 1892, p. 104.

In the anterior fissure and at the roots of origin of the anterior nerves cellular elements, largely of the small round cell variety, were abundant. With these were also found other cells in small number—large inclusive cells, cells with vesicular nuclei, and polynuclear leucocytes. On the posterior aspect of the cord the surface exudate and the injection of bloodvessels and membranous infiltration were more decided than on the anterior aspect, and the posterior fissure contained a larger amount. The body of the cord was invaded in like manner, but to a greater extent than in front. That part of the cord at which the posterior roots enter was especially the site of cellular infiltration; between the roots and the median fissures the cell infiltration was abundant, but a uniform layer of cells may be said to have extended from the anterior lateral to the posterior lateral fissure. The predominating cells resembled "lymphocytes or the mononuclear cells of granulation tissue."

Changes in the ganglionic cells of the cord were not marked; some variation was observed in the granulation of the cells and in the clearness of the nuclei and nucleoli, and especially in the sharpness of the cell outline. There were no well defined changes in the axis cylinders of the cord observed by Flexner and Barker, owing possibly to some difficulty in satisfactorily staining those parts. In the nerve roots, however, swelling of axis cylinders and interstitial changes also were marked.

In both anterior and posterior roots the axis cylinders were swollen in considerable numbers, though in the anterior roots a large number—the majority—were not affected.

"The normal axis cylinders lie in a space which has apparently been formed either by the disappearance in part or the contraction of the myelin sheath, a faint line of myelin being still visible just inside Schwann's sheath; in some instances the myelin entirely fills the space between the axis cylinder and the sheath of Schwann. On the other hand, the swollen cylinders, which occur singly or in groups, always fill the space inside the myelin sheath, being distinguished from the latter by their larger size and by their staining properties. It is worthy of note that in those nerves in which a cellular proliferation, especially around the veins, can be made out, more axis cylinders show this change than where the cellular increase is not so apparent."

The vessels of the perineurium are engorged and hemorrhages occur between the bundles. Cell proliferation in the interstitial tissue is not abundant in the anterior roots, but in the posterior roots it is quite marked, and at times is so great in the peri- and epineurium as to obscure the fibres. Other organs are more or less affected, but not in a manner distinctive of the disease. Congestion of the kidney, liver, spleen, and lungs with œdema not infrequently occurs.

The lungs are at times engorged, œdematous, or solidified, and the pneumococcus is found in the exudate.

The pleura and pericardium are now and then inflamed and ecchymotic, and occasionally lined with purulent exudate. Endocarditis is also occasionally present. v. Ziemssen has found the intestine presenting conditions analogous to those occurring in dysentery.

Effusions into the joints, purulent or semi-purulent, are not infrequent.

Granular degeneration of voluntary muscles, especially of the spinal muscles, is of common occurrence.

SYMPTOMS.—The period of incubation is necessarily uncertain, if indeed there is any propriety in speaking of an incubative period in a disease supposed to have its origin in an organism almost uniformly present in the human body. Whether the organism begins to acquire virulent properties or the body ceases to be resistant to it cannot at present be stated, since we know so little of the circumstances effecting the change. Nevertheless, persons have been known to develop symptoms after association with the infected or after exposure to contact with infected clothing within from eight to ten days.

The symptoms are necessarily varied and complex, depending as they do on the degree of toxæmia, the extent and site of the inflammation, and the amount of inflammatory exudate, and this irrespective of the particular organism concerned in its production.

Certain cases progress with such rapidity and violence as to overwhelm the system before the local changes can exert marked influence. Others present phenomena of the gravest character, which may be altogether ascribed to profuse exudation in and upon delicate structures within a circumscribed space surrounded by unyielding walls; still others to the direct destructive metamorphosis of the inflamed tissues.

To what extent any of the clinical features of the disease are due to the local action of the infecting organism cannot now be said, since but little is known of this branch of the subject. It may be stated, in general terms, that the psychical phenomena are most apparent in those cases in which the cortex is most implicated, the special sense disturbances where the base is most involved, and the muscular and general sensory disorderly manifestations when the spine is extensively invaded.

The fact must not be lost sight of that all the phenomena characteristic of this affection may occur without any inflammation of the meninges whatever—that decided inflammation of considerable extent and with abundant purulent exudation over convexity and base may be revealed post-mortem in cases where no clinical evidence of its existence had been present, as in a case related by L. Emmet Holt.[1]

Prodromata are exceptional, and when present not very characteristic. Occasional rigors, general malaise, headache, back-pain, vertigo, and loss of appetite furnish little if any indication of the nature of the impending trouble.

No elaborate classification of the varieties of the affection is desirable. It is sufficient to describe the ordinary form, and to note the particulars in which it may vary from this form, and as far as may be the condition causing or attending such variation.

The Ordinary Form.—Prodromata are rare and slight, such as have already been referred to. It has been thought that cerebro-spinal meningitis is more likely to begin between the hours of midday and midnight. Since the epidemic of 1872, 36 recorded cases. J. Lewis Smith says, were almost without exception in this particular, from which he concludes that the comfortable sleep and rest of the latter part of the night increases the resistance of the body to the disease. Although fatigue is a recognized factor in predisposing to this affection, yet this view seems somewhat fanciful, nor is it practicable to say in any large number of cases at what hour the disease begins. Rigors are occasionally initial, but by no means characteristically so. Pain in the head is an early and continuous symptom. It may be over the brow or at the back of the head, most frequently in the latter position. The site of the pain does not necessarily indicate the site of the inflammation: it may be upon one side, while the inflammation is on the other. Nor does the degree of pain have any constant relation to the intensity or the extent of inflammation. It extends down the neck and back, and is accompanied by intense hyperæsthesia. It is decidedly increased on motion, and is usually associated with rigidity of the muscles of this region, ranging from simple stiffness to marked tetanic contraction, with extreme pain and decided opisthotonos. Both the pain and contracture in the cervical and dorsal region are doubtless due to the involvement of the posterior nerve roots, although the contracture may be in part the direct effect of the inflammation of the anterior roots.

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[1] *Transactions of the American Pediatric Society*, vol. v. p. 214.

In perfect repose of body there may be considerable periods of immunity from pain, but any attempt at movement is attended by its recurrence. The extreme extension of the spine is in part due to the rigidity, and in part to the desire of the patient to relax the affected muscles. The same condition and purpose doubtless prompt the flexion of the thighs on the pelvis and the legs on the thighs, a position very commonly assumed by the patient.

The arms are also flexed at the elbows and on the chest. These muscular contractions may be in part due to voluntary effort to lessen the tension of painful muscles, but is to a greater extent reflex, indicating irritation of the sensory roots or perhaps direct irritation of the anterior roots, or to a combination of these. A sense of thoracic constriction with respiratory difficulty is very frequently present in cases without pulmonary complications, and serves to show how independent of volition the muscular phenomena may be. In this connection may be mentioned Kernig's sign, which he believes distinctive of this disease. He observed a flexion contracture of the knee joint, which in the sitting posture could not without violence be straightened beyond an angle of 135° with the thigh, but which was readily straightened when the patient was in the erect or recumbent posture. It is objected to the pathognomonic character of this symptom that it may also be observed in chronic alcoholism, old age, etc., but Kernig has examined several thousand persons especially for it without finding it in a single instance except in cerebro-spinal meningitis. Pain in the sacral region and loins and in the joints is not uncommon. It is much more frequent and severe, however, in the head and cervical and dorsal spine. Whether the pain be present or not, muscular rigidity commonly is, and is most decided in the same regions of the spine. With the cephalalgia vertigo is frequently associated or may occur independently of it.

In children the disease may be ushered in with convulsions which may recur repeatedly during its progress until it finally ends in coma and death. In all severe cases convulsions are liable to occur in the later stages, and patients usually pass into a comatose condition before death. The convulsions have no necessary relation to the site of the inflammation (Gowers). When they are of frequent occurrence and the patient remains in a state of stupor in the intervals, they commonly indicate a fatal termination.

Delirium is frequently present, and may be active and continuous or may be succeeded by stupor, which in turn gives place to active delirium when the patient is aroused.

The tendon reflexes are usually increased during the period of irritability and diminished in the later period. The cutaneous reflexes are exaggerated. Choreiform movements are occasionally present, and may issue in a true chorea lasting for months.

With the headache is heightened sensibility in the special sense organs, evidenced by intense photophobia and increased suffering when noises invade the room of the patient. Aversion to light and sound is at times extreme in the early stages, and gives place to indifference as the products of inflammation increase, and the affected nerves or their centres become structurally more and more impaired until their function is partially or completely abolished. With the photophobia also coincides the muscular rigidity of the eye muscles, giving rise to strabismus, irregular movements of the globe and eyelids, and contraction of the pupils, to which succeed nerve and muscular degeneration, with paralysis, ptosis, dilatation of pupils, and blindness.

Nearly all cases of cerebro-spinal meningitis are attended with marked and obvious changes in the eye. Besides the nervous and muscular symptoms already alluded to, there may be lesions of every portion of the structure of the orbit. Keratitis occurs in many instances, giving rise to opacity of the cornea, followed by blindness (Wilson, Niemeyer). Iritis and choroiditis resulting in blindness are not infrequent. Knapp reports that in the epidemic of Rastadt near Heidelberg from 4 to 5 per cent. of cases were affected with what he considered a hyperplastic choroiditis with consecutive retinal detachment and iritis. Krietmar and Salomon after an examination respectively of 15 and 6 cases affected similarly—that is, with subconjunctival injection, œdema of mucous membrane of eyeball, hypopyon, discoloration of iris with redness of lids which lasted one or two weeks, leaving the eyeball soft and the patients blind—looked upon it as a simple irido-choroiditis.

Randolph[1] found the eyes more or less affected in nearly all cases. Engorged and tortuous retinal veins, enlarged papillæ, and optic neuritis were the conditions commonly noticed by this observer. In one instance thrombosis of the central vein was seen. This condition has been observed by Michel, who recognizes three varieties, "complete, incomplete, and slight" thromboses. In even the third variety marked stasis occurs, recognizable by the dark red color of the blood and the tortuosity of the venous branches. Age and the associated atheroma seem to play an important part. Michel's 7 cases ranged from eighty-one to fifty-one years, and were sometimes associated with cardiac ventricular hypertrophies. Embolism of the central artery due to the same causes and occurring also in elderly patients is not uncommon. Popp reports 50 cases, all over twenty-one years of age. Blanco reports from Galezowski's Clinic an average age of forty-eight years. Randolph thinks his one of the youngest cases recorded—twenty months—and thinks it belongs to the phlebitic form as distinguished from the marantic, which is seen only among elderly persons. This writer calls attention to the important fact that the eye phenomena may be detected ophthalmoscopically some time before there is subjective evidence of such severity as to attract attention in the midst of the severe general suffering. Of the 35 cases examined by Randolph, the fundus was normal in but 7, and of these 7, "1 had divergent strabismus and dilated pupil, another had marked nystagmus, and still another had greatly dilated pupils." In 6 were optic neuritis; in 1 retinitis with thrombosis of the central vein; and in 19 cases there were great venous tortuosity and engorgement with congestion of the optic disk. The right eye was much more frequently affected than the left.

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[1] Robert L. Randolph, *A Clinical Study of Forty Cases of Epidemic Cerebro-spinal Meningitis, with reference to the Eye Symptoms.*

Randolph considers the conditions here noted as of great gravity in prognosis, far more so than panophthalmitis, suppurative choroiditis, and keratitis—conditions more commonly described by other writers.

The tongue, teeth, and lips are at times covered with sordes. Vomiting is an early severe and often persistent symptom, and appears to be reflex in character rather than due to any direct lesion of the gastric mucosa. It is not usually associated with decided nausea, nor is there any especial tenderness on pressure over the stomach. Difficulty in swallowing occurs, and the effort of swallowing and the body movement connected therewith may bring on vomiting and muscular contractions, and to this, in part, is due the apparent lack of appetite in many cases. The desire for food may be normal or nearly so, and yet the difficult deglutition and the apprehension of tetanoid seizure on rising for the purpose of swallowing will cause children, who can give no explanation, to decline food in many instances.

The bowels are more often constipated, but diarrhœa is not infrequent, and occasionally dysenteric stools with mucus, blood, and tenesmus are present. In the later period involuntary stools may occur, sometimes unconsciously, at others with the knowledge of the patient.

Pyrexia is irregular, following no definite curve. It is not usually very great, ranging in the neighborhood of 102–103° F. or lower, and is at times subnormal. Nor does the temperature bear any close relation to the severity of the disease. The variations are abrupt and marked without apparent reason in the severity of other symptoms. Indeed, it seems necessary to assume some direct effect on the heat centres. At times there is no fever, but this does not always justify a favorable prognosis: just before death it may reach 108–109° F.

Herpes facialis is often present, and a petechial rash is quite common. One of the most common eruptions observed in the Lonaconing series was "an indistinct purplish mottling that appeared and disappeared almost under the eye." Many cases are unattended with eruptions. The contribution to the study of this disease by Flexner and Barker is especially interesting in the careful study of the blood which they were able to make, a line of investigation hitherto almost neglected.

Halle and Von Limbeck found a leucocytosis in suppurative meningitis, and Riedar observed two cases of epidemic cerebro-spinal meningitis, one having 20,100 white corpuscles, the other 17,500 to the cubic millimetre. Flexner and Barker thus epitomize the result of their examinations: "In the fresh blood slide no marked variations in size or shape of the red corpuscles could be made out; in some of the cases, however, there was distinct pallor of the red cells. The increase in the number of the leucocytes was quite evident in many cases in the examination of the fresh drop of blood, and a greater number of white corpuscles appeared to be motile than one sees under normal conditions. Many of the leucocytes presented a striking vacuolation—a condition which, we believe, is not uncommon in the leucocytes dependent on other causes. The blood platelets were present in lumps, but did not appear to be decidedly increased or diminished in numbers."

As to the number of corpuscles present, the average of a number of counts shows that a diminution of the red cells is not a marked feature of the disease. In some of the advanced cases, with emaciation there was "a moderate oligocythæmia, but in the majority of instances the full complement of red corpuscles was present. The hæmoglobin, however, in all cases examined was somewhat diminished in amount, so that the individual corpuscular holding in hæmoglobin (valeur globulaire) was below par. A well marked leucocytosis is, we believe, a constant phenomenon in the disease during its active stages. In no case examined, except in convalescent patients, was it absent. The number of white corpuscles varied in different cases in our experience between 12,000 and 32,000 to the cubic millimetre. That the degree of variation is greater, however, there can be little doubt, and it is probable that further investigations will prove that still larger leucocytoses may exist, especially in cases of meningitis associated with complications in the lungs or joints."

These changes in the blood are not peculiar to meningitis, but common to suppurative inflammations. No micro-organisms were found in it.

A decided variation in the proportion of hæmoglobin was observed in several of these cases, amounting to from 45 to 74 per cent. In two cases the percentage was 45 per cent. and 55 per cent. respectively, without material diminution of the number of red corpuscles, but both had shown chlorotic symptoms prior to the meningeal inflammation, and the diminished number of red corpuscles was therefore probably not dependent on it.

No characteristic respiratory difficulty occurs in epidemic cerebro-spinal meningitis, though the respiration is often irregular, sighing, or of the Cheyne-Stokes type, and in convulsions and coma presents the peculiarities that belong to these conditions. General cyanosis happens quite often.

Epistaxis was of frequent occurrence in the Lonaconing cases.

The pulse presents nothing so distinctive as its irregularity. It may be quick and feeble or slow and intermittent. Endocarditis is rare, and may rather be considered a complication than a symptom.

Joint swellings with pain are frequently observed and seem to characterize particular epidemics.

The urinary function is commonly but little disturbed. Polyuria is present at times. Albumin may be present, and occasionally a few casts are found. The urine is often of high specific gravity and contains an excess of phosphates. The diazo reaction was obtained by Ehrlich in severe cases. There is also at times retention of urine from irritability of the sphincter or from paralysis of the detrusor muscles.

Emaciation is characteristic of this disease, and is at times extreme. It may be accounted for, in part, by the great suffering, loss of appetite, and vomiting, but is doubtless to a greater extent the effect of trophic disturbance due to the central lesions and to the direct influence of the toxins upon the blood.

The early stages are characterized by symptoms of exaggerated nerve sensibility, pain, general hyperæsthesia, photophobia, aversion to sound, irregular and forcible muscular contractions, delirium, and convulsions, to which succeed symptoms of nervous exhaustion or structural impairment, such as cessation or diminution of pain, indifference to light, with dilated pupils, blindness, deafness or indifference to sound, muscular paralysis, coma, and death.

A form of the disease characterized by extreme severity of all symptoms and rapid progress to a fatal issue is known as fulminant (*meningitis cerebro-spinalis siderans, méningite foudroyante*). The patient quickly becomes comatose, and may expire in twenty-four hours or less. These explosive cases can only be explained by assuming an overpowering effect on the nerve centres by the toxic agent. They are the cases which show the smallest amount of inflammatory exudate and but slight structural changes. To them cannot be applied the statement of Leyden, that the gravity in many cases is due rather to the effects of the exudate than to the severity of the infection.

In the Lonaconing epidemic, cases of this type were relatively quite frequent; no less than 10 patients died within forty-eight hours; one child died in eight hours, and another in ten hours. In the less violent cases death ensued in from six to fourteen days. In Pepper's *Text-book*[1] a case is mentioned in which death occurred in five hours. These cases may be entirely without fever, or the temperature may be subnormal, with cyanosis and a cold clammy skin. The symptoms are essentially the same as in the ordinary form, except for the rapidity with which they develop. Delirium is early in appearing and quickly passes into coma. Rarely does any improvement occur and recovery is almost unknown.

Remission of nearly all severe symptoms at times takes place, and at times complete intermission, so that an intermittent form is recognized. After a brief period of subsidence all the symptoms may return with equal or increased violence, but the intervals are not so definite nor does the fever pursue the same regular course as in intermittent fever.

Abortive cases are also recognized in which the disease may be ushered in with the usual symptoms, often of considerable severity, and after a brief career terminate suddenly to recur no more. The meningeal inflammation in these cases is probably slight.

COMPLICATIONS AND SEQUELÆ.—Severe cases are not uncommonly followed by sequelæ of a grave character—blindness due to changes in the optic nerve or its exhaustion, or at times to injury done the cortex by inflammatory infiltration or by pressure from large exudates. This may also result from opacities of lens or cornea.

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[1] *An American Text-book of the Theory and Practice of Medicine*, Pepper, vol. i.

Deafness brought about in like manner is of frequent occurrence. Paralysis of orbital muscles with defective movements of the eye or permanent strabismus, ptosis or more general paralysis of one arm, leg, or the entire side, may ensue. The higher psychical functions may suffer such impairment as to leave the patient permanently imbecile. Children may be left deaf and dumb, imbecile, and paralyzed for long periods or for life. Deafness is perhaps the most common of the sequelæ, and is often due to destruction of the middle ear, and with it vertigo may be associated from involvement of the semicircular canals.

Pneumonia is frequently associated with meningitis, and it may often be questioned which is the primary disease. The same organism appears to be responsible for both the pulmonary and meningeal affections. Bronchitis, pleuritis, endo- and pericarditis may be occasional complications or sequelæ.

Malignant or infective endocarditis stands in especially close relation to epidemic cerebro-spinal meningitis. Osler[1] in 103 autopsies in acute pneumonia found 11 cases of malignant endocarditis, among which were 5 of meningitis. In 14 cases reported by Byron Bramwell[2] there was croupous pneumonia certainly in 2, and probably in 7. Osler and Jaccoud have pointed out that in these cases of endocarditis there is not always a loss of tissue, but sometimes a proliferation, and this M. Sée thinks is peculiar to the pneumococcus cases, while the ulcerative form arises from the streptococcus. Trevelyan[3] holds the opinion that the same organism under one set of conditions may produce meningitis, under another endocarditis, in another pneumonia or any combination of these. A persistent headache, often lasting for months, may be regarded as among the more common sequels. Chronic hydrocephalus, indicated by mental feebleness, loss of control over the sphincters of bowel and bladder, vomiting, pain in head, back, and extremities, loss of consciousness and convulsions, is, according to v. Ziemssen, not rare.

Some cases of epidemic meningitis are indefinitely protracted, constituting a chronic form. I am inclined to agree with Pepper that these protracted cases are commonly due to some persistent or progressive lesion, such as chronic meningitis, chronic hydrocephalus, or even abscess of the brain.

CAUSE OF DEATH.—Death may occur in many ways—in the ordinary form probably most often from asthenia due to continuous suffering, sleeplessness, inability to take or retain food, or to bed-sores with exhausting discharges. Death from this cause may be at a tolerably early period, since the joint result of the causes enumerated tends to speedy exhaustion, or it may be deferred many months.

Death may also result from profound toxæmia overpowering the nerve centres prior to any sufficient intracranial local results of inflammation. This, apparently, is the manner of death in the foudroyant form when it occurs within the first week or ten days.

Again, it may be immediately due to the mechanical effect of inflammatory exudates or to the structural changes wrought in the inflamed nervous elements by the spreading of the inflammation inward, and not the mere pressure of fluid; but we cannot think this the most common cause of death, or, at any rate, that it gives sufficient warrant to the statement that death is due to the local intracranial mischief rather than to the infection *per se.* Not a few cases must also die in consequence of complications, such as pneumonia, superadding pulmonary obstruction to central respiratory labor. A few cases with nephritic complications may have a fatal issue determined by addition of uræmia to the other depressing influences. Fatal results sometimes occur many months after apparent recovery, or patients may continue ailing many, many months before death ensues. Hadden's case lasted over fifteen months, and Strümpell[1] reports a case that died after three months' illness.

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[1] *Gulstonian Lectures*, 1885.

[2] *International Journal of Medical Science*, 1886.

[3] Trevelyan, *Brain*, part 1, p. 109, 1892.

DIAGNOSIS.—Owing to the extremely varied clinical picture presented by this disease, in sporadic cases it will often escape recognition, but during its epidemic prevalence, when it is in the thought of the observer, it can usually be readily diagnosed. A primary difficulty occurs in the fact that all the characteristic symptoms may be present in the absence of any meningeal inflammation whatever, as in the case of middle-ear disease, and this difficulty is increased when it is remembered that middle-ear inflammations may excite meningitis or a primary meningitis may lead to suppurative otitis. Time and treatment of the aural affection can alone resolve the doubt in such cases.

The positive indications of meningitis are sudden invasion, pain in head, cervical, dorsal, and lumbar regions, loins, and less often of the extremities; intense general hyperæsthesia; assumption of positions relaxing painful muscles; great increase of pain on movement; inability to effect extension of the legs in the sitting posture, which may be readily effected in the recumbent posture; petechiæ, purpuric spots, herpes labialis, vomiting, and intense photophobia with irregular movements of the globe.

Ophthalmoscopic examination of the eye will almost always show some orbital lesion even in advance of subjective indications. Engorgement and congestion of the optic disks, venous thrombosis, tortuosity of veins, descending neuro-retinitis (von Graefe), are conditions frequently present and of great value in diagnosis, as are also intolerance of sound, delirium, stupor, irregularity of pulse; and, finally, blindness, indifference to sound, paralysis, and coma.

The disease is to be differentiated from typhoid fever, in which the cerebral symptoms are a prominent feature. Typhoid is more gradual in its invasion, the fever pursues a more definite course, the pulse is more regular and uniformly rapid, pain is less pronounced and more apt to be limited to the first stage, vomiting is much less frequent, bending and rigidity of neck and back are rare, sordes on tongue, lips, and teeth is more often present and usually in greater quantity. The rose spots of typhoid are distinctive when present. Ileo-cæcal gurgling and tenderness, and after the first week looseness of the bowels, are more distinctive of typhoid. Epistaxis and intestinal hemorrhages are common to typhoid. Delirium is less active usually, and stupor more continuous. When hyperæsthesia is present in typhoid it is of brief duration. Extreme photophobia is rare in typhoid, as is also the great sensibility to sound.

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[1] *Pathological Society Transactions*, 1885.

Typhus fever resembles epidemic meningitis in the abruptness of its invasion, the extreme headache and cervical pain, general hyperæsthesia, and rapidly developing delirium and stupor. It differs in the briefer duration and commonly milder character of the pain and muscular rigidity. The hyperæsthesia is less : great photophobia is uncommon. The fever is more uniformly high in typhus and pursues a more regular course. Typhus in this country is more rare, is virulently contagious, and can commonly be readily traced to its origin. The roseolous eruption in typhus is tolerably constant to the fourth day, while the eruption of meningitis may occur on the first or second day. Herpes rarely if ever occurs in typhus.

Kernig's sign, of which we have no personal knowledge, according to its discoverer serves to distinguish cerebro-spinal meningitis from all other affections.

Influenza has some points of resemblance to meningitis, more especially the sudden invasion, the head and back pain, convulsions, and stupor; but the absence or mildness of muscular rigidity, the rarity of delirium and coma, the presence of catarrhs, the relative mildness of the special sense symptoms, and its cosmic prevalence serve sufficiently to distinguish it. The cerebral type of influenza which most closely resembles epidemic meningitis usually occurs as an occasional variety during the prevalence of other forms.

The presence of the grip organism may serve to establish the diagnosis, or, rather, we should say, to establish the etiology of the particular case, for a true meningitis may exist differing in no important particular from that induced by any other cause. Gowers thinks that meningitis, especially the tubercular form, is not rarely confounded with hysteria, from which it may be distinguished in part by the previous history of the case. Hysterical attacks are rarely single and the individual symptoms are seldom persistent. Hysteria commonly belongs to a later period of life, and more especially to the female. Strabismus in hysteria is always convergent, associated with contracted pupils, and varies from day to day. Strabismus due to organic disease is always divergent and connected with irregularity of pupils. Pyrexia and the existence of trophic disturbances of the skin make for meningitis.

The presence of symptoms distinctive of organic disease, such as the ophthalmic conditions referred to, are of far more value in diagnosis than the history of previous attacks, and go much farther in favor of meningitis than a history of previous attacks goes in favor of hysteria.

From other varieties of meningitis the epidemic form is not to be positively diagnosed by the symptoms alone. In all forms of meningitis the direct structural results of the inflammation are the same, and the pressure effects of the exudate are not different. So likewise in ordinary cases the toxic effects are not clinically distinguishable. It is only in fulminant cases, which may be said to be peculiar to the epidemic type, that any marked clinical distinction exists, and this chiefly in the sudden and violent manner in which the symptoms develop. Just, however, as ordinary epidemic cerebro-spinal meningitis differs from the fulminant variety in the slowness and relative mildness of its development, so does tubercular meningitis usually differ from ordinary epidemic meningitis in the comparative slowness of its advance. But it is more to be distinguished by the history of tuberculosis in the family and other tubercular manifestations in the patient, especially by the presence of tubercular choroiditis, a previous history of pleuritis, or a strumous condition of glands or bones.

Herpes makes for epidemic meningitis, as it is rare in the other forms. Next to the recognition of other tubercular processes in the patient or other members of the immediate family, of most value in differentiating them is the prevalence of an epidemic of meningitis. Muscular contractures and hyperæsthesia are usually of milder type in the tubercular form. It also runs a more protracted course and is more assuredly fatal. It is also much more apt to involve the base and to present symptoms indicative of its site.

Smallpox, scarlet fever, rheumatism, and other diseases are mentioned by writers as representing features of similarity, but they are so unlikely to be mistaken for epidemic meningitis that it is scarcely necessary to consider them in detail. Pneumonia is at times primary and at times secondary to meningitis, but as it seems probable that they have a common origin it matters little which is the antecedent disease. There is of course no difficulty in distinguishing between the inflammation of the meninges and a pneumonitis.

Tetanus might possibly be confused with sporadic cases of meningitis, but the diseases are readily distinguished by the history of injury in the former, the more violent muscular contractions and the consequent deformity, the persistent presence of trismus, the greatly exaggerated reflexes, the diminished sensory disturbance, the absence of photophobia, and the freedom from mental disturbance.

PROGNOSIS.—The prognosis is always grave, and, though many cases doubtless recover, of no case is it possible to anticipate recovery with any strong measure of probability. The mortality varies in different epidemics, but is always high, ranging from 30 per cent. to 70 per cent., according to v. Ziemssen ; Hirsch places it at from 20 to 75 per cent. In the mild or abortive cases recovery may take place in five or six days. But in other forms it is the more protracted cases that do best : those that live past the first week have a moderately fair prospect of recovery, but as it cannot be said of any case, however mild in the beginning, that it will recover, so it cannot be said even in cases advanced to the stage of coma that they are quite hopeless. In all, however, in which the onset is sudden, the symptoms violent, the stupor persistent, the pupils dilated, the muscles paretic, the pulse feeble and irregular, the skin cyanotic, death may be confidently anticipated. Cases advanced to the stage of coma have recovered, but so rarely that this condition may be taken as of fatal significance. Under five and over forty years are unfavorable periods. All fulminant cases die, or the exceptions are so few they may practically be left out of consideration.

TREATMENT.—There is no specific treatment for epidemic cerebrospinal meningitis, and no very effective symptomatic treatment. In all cases the patient should be placed in a cool, darkened, and well ventilated room, from which all visitors and noises are to be rigidly excluded. The

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severe purgation was followed by recovery seemingly due to the remedy. Such remarkable effects, however, are not to be anticipated, and the measure is undoubtedly capable of harm in enfeebled subjects.

Calabar bean, recommended by N. S. Davis, is entitled to further trial: as yet but little evidence of its efficiency is offered.

In a disease in which we know of no means of destroying the organism producing it, nor any of neutralizing its toxins, which runs a rapid course to a fatal issue in a large proportion of cases, it would seem most advisable to limit our efforts to the relief of symptoms, the maintenance of strength, and to those topical measures which are under other circumstances found to limit the amount of inflammatory transudation.

All of these purposes are in a measure accomplished by anodynes, of which opium and its derivatives are best. The most troublesome symptoms are pain, hyperæsthesia, muscular spasm, vomiting, sleeplessness, and all of these are more effectually combated by the hypodermic injection of morphine than by any other means. In the later stages, when coma supervenes, neither this nor any other measure is likely to be of any use, and it is only at this period that there is danger in the discreet use of this agent. It is a conservator of strength, since nothing conduces to speedy exhaustion more than continuous suffering, loss of sleep, and inability to take and retain food. So far as any drug does, it lessens the amount of inflammatory exudate, and in those cases in which the progress of the case is uninfluenced by it, it more than any other agent solaces the last hours of the sufferer.

Of equal or perhaps greater value is the coincident use of cold to the head and spine. To be useful it should be thoroughly used, and the best results are to be had from the early and almost continuous application of ice to these parts. This measure likewise lessens pain, diminishes transudation and the migration of leucocytes, overcomes muscular spasm, relieves vomiting, especially if ice is also kept in the mouth and occasionally swallowed, and conduces to sleep. This measure may be advantageously associated with the application of warmth to the extremities; and, since its good effect is probably largely due to the diminution of cerebral and spinal hyperæmia, we may reasonably expect that coincident lowering of the general blood pressure by the administration of such agents as nitroglycerin will materially favor this end.

As the general temperature is not usually very high, and lifting or other manipulation of the patient is very painful and likely to produce muscular spasm, the use of cold bathing is contraindicated; moreover, by inducing contraction of the cutaneous vascular area it would tend to heighten the blood pressure in internal organs. Applications of ice to the head and spine as directed are far less troublesome, less painful, more efficient, and probably unattended by the ill effect referred to.

Cold douches to the head or the use of a Leiter's coil where ice cannot be had may be advantageously employed, but they are not of the same efficiency as the continued application of ice.

Aufrecht[1] reports a case of cerebro-spinal meningitis with low temperature treated with hot baths, 40° C., with immediate remission of symptoms and subsequent recovery. His patient was a man twenty-five years of age, in whom, at the end of the third week of illness, benumbed sensorium, constant delirium, and persistent opisthotonos existed. The pulse was rapid, but the fever had subsided. "After the somnolence had lasted ten days, in view of the frequent pulse and low temperature it was decided to use the hot baths. There were given from the 15th to 17th of April twelve baths at 40° C. of ten minutes' duration each. After the first baths improvement began. Gradually the sensorium cleared up, pain and opisthotonos diminished, incontinence of urine and fæces disappeared, the abducens nerve assumed its normal function, and the power of speech returned. Upon discontinuing the treatment nocturnal headache and delirium reappeared, whereupon three more baths were given, after which all symptoms of disease vanished."[1] This very interesting case suggests a wider field of usefulness for hot baths than within the clinical limitations mentioned. That hot baths may be useful in the absence of fever, with feeble pulse, clouded sensorium, and headache, need surprise no one; but remembering the great hyperæmia in all stages of this disease of the vessels of the brain and cord, the extent of the inflammatory exudate within the cranium and spinal column, and the not infrequent congestion of other internal organs, it would be perfectly rational to expect benefit in other cases in which the temperature was not very high, even, or perhaps most, in the early stage of this infection. Hyperpyrexia rarely occurs in this disease except just before death.

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[1] *Die Therapie der Gegenwart*, Jan., 1895.

Indeed, high temperature is not a characteristic of cerebro-spinal meningitis, and may in many, if not most, cases be ignored if measures which might add to the pyrexia tend to the relief of other more important conditions; and probably nothing is more important than the diversion of blood, if it can be effected, from the engorged cerebral and spinal vessels, and no measure seems better calculated to effect this than the measure under consideration. It may also be serviceable by favoring the elimination through the sweat glands of toxic agents; and also, by lessening nephritic hyperæmia, increase the functional activity of the kidneys with a like result. It would, moreover, in the judgment of the writer, be rational to associate this with the application of ice to the head and over the carotid arteries; and, if the reasoning is just, these measures are especially applicable to the early stage of the affection before injury, mechanical or other, is done to the important structures implicated.

Other remedies of anodyne and hypnotic properties, such as potassium bromide, chloral hydrate, sodium bromide, bromoform, phenacetin, and chloroform, are at times useful, but none of them are so potent for good as morphine in cases where it is well borne. The writer has seen phenacetin give the most marked relief to the painful symptoms and induce quiet and restful sleep in other forms of meningitis, and should be inclined to expect similar benefit in the epidemic form. Iodide of potassium has long enjoyed some repute as a sorbefacient in this affection. In syphilitic cases and in subacute and chronic cases, after the subsidence of acute symptoms, it may be of some value, but in the career of the disease it can be of little service. Its value at any time when syphilis does not complicate the trouble has doubtless been exaggerated. The use of quinine has been advocated, but it is of doubtful advantage, nor is there any reason to suppose it more useful in the intermittent cases than in others.

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[1] *Journal of Nervous and Mental Disease*, March, 1895.

To maintain the strength of the patient careful attention should be given to the food. It should always be liquid, and should be administered at short intervals. If the vomiting makes it difficult to retain the food, advantage may be taken of an administration hypodermically of morphine to give a somewhat larger quantity than at other times. The use of chloral hydrate by enemata will often relieve this symptom for a time and enable the patient to retain food. Rectal feeding may also be practised with advantage, in which case the food should always be peptonized. The writer is skeptical as to the benefit of forced feeding in troubles of this kind. The use of a stomach tube is very likely to induce efforts at vomiting. The struggle necessary for its introduction must add to the pain in head and back, produce severe muscular contracture, and in the young and timid convulsions may be excited. The free use of water at such temperature as best suits the patient, if it can be retained, is always desirable. With little children the white of an egg may often be given mixed with water, slightly sweetened and acidulated with lemon, without exciting opposition, to the manifest advantage of the patient. Animal broths in all forms may alternate with milk and eggs. The administration of stimulants may become needful, especially when food is badly assimilated. At times a little champagne iced or brandy and ice will quiet the stomach, and enable food to be retained better than anything else. When they add to the excitement of the patient, increase the pain and delirium, or notably heighten the fever, it is best to omit them. Milk punch by stomach or bowel is a good form in which to give alcoholic stimulants. At all times when there is great depression and a feeble heart they may be tried, subject to the above conditions.

In cases that recover convalescence is often protracted and requires the careful supervision of the attendant. Stimulants may be required, but if food is taken in fair quantity and appears to be well digested and assimilated, alcohol may be advantageously dispensed with. Active exercise is commonly impracticable, but passive exercise in the open air and sunshine should be enjoined as soon as it can be borne without distress. Massage of paralyzed muscles and of stiff and painful joints will be of service. With this electrical stimulation may be associated to advantage.

Various drugs are recommended during this period, such as mercury and potassium iodide to favor absorption of inflammatory products, iron, cod-liver oil, bitter tonics, etc. Good food when it can be digested and assimilated is the only real tonic, and drugs of this class are only valuable in so far as they favor these ends. It is to be feared that in the majority of instances they are more likely to disturb the stomach and impair digestion than to improve it. Perhaps a few drops, not above five or ten, of the muriated tincture of iron, with a slight excess of hydrochloric acid, especially in cases where this acid is shown to be deficient in the gastric secretion, taken directly after meals, will at times prove of value. But so far as drugs are concerned it may be said without reservation that no drug that disturbs the stomach can at this time be other than harmful, and no matter what the supposed indications for its use it should be withheld. With these may be classed even those peptonized and other artificially digested foods which offend the taste and nauseate the patient. Sapid foods that "make the mouth water" also excite the gastric secretion, and are, other things being equal, most easily digested. There can be little doubt that enjoyment of food has much to do with its proper digestion, or, at any rate, food that offends the taste or has merely lost its savor by reason of sameness is less likely to be promptly digested. As much variety should therefore be secured as is practicable. It is much to be feared that lack of suitable seasoning is too often a characteristic of sick-room diet. Insipidity in food with defective taste in the invalid is an unhappy conjuncture. As there is no local inflammatory trouble in the alimentary canal, in these cases there can be no reason why pungency in food should be objected to if it accords with the patient's taste.

ERYSIPELAS.

BY GEORGE DOCK, M. D.

SYNONYMS: Rose, St. Anthony's fire; Érysipèle (French); Erysipel, Rothlauf (German), etc. The etymology is uncertain.

DEFINITION.—Erysipelas is an acute infectious disease characterized by a peculiar inflammation of the skin, with fever and other general symptoms, and caused by the streptococcus of Fehleisen.

ETIOLOGY AND PATHOLOGY.—Formerly considered a so-called general disease caused by alterations in the body fluids, especially bile (Galen to writers of the nineteenth century[1]), with a local manifestation, we now know that erysipelas is of bacterial origin, beginning as a localized infection and producing general symptoms as the result of the local disease. Very early in the history of bacteriology[2] bacteria were found in erysipelatous lesions, but their constant occurrence was first shown by Koch.[3] About the same time, and independently, Fehleisen[4] not only demonstrated the presence of the organisms, but by cultures and subsequent inoculations showed their causal relation. The inoculations included seven on human beings, the subjects of inoperable malignant disease, and justified by the clinical observation that erysipelas acquired in the ordinary way in such cases seemed sometimes to have exerted a favorable influence.

The streptococcus of Fehleisen was supposed at first by its discoverer and others to be *sui generis*, and it was not until several years after the first announcement of Fehleisen, when the value of the independent researches of Rosenbach, Passet, and Garrè on pyogenic streptococci could be realized, that the specific nature of Fehleisen's organism was seriously questioned. Since then, as the result of an enormous amount of experimental and much clinical work, the belief has gained acceptance that the streptococcus of erysipelas is identical with the *streptococcus pyogenes* of Rosenbach, and cannot be distinguished from the streptococci found in suppurative lesions of the most diverse kinds—*e. g.* phlegmon, puerperal peritonitis, certain anginas, etc.

A discussion of the various observations and experiments for and against the specific nature of the erysipelas organism is quite outside the object of the present article. Much confusion has been thrown around

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[1] *E. g.*, "There are a number of reasons which make it extremely probable that the connection between the skin and mucous membrane of the alimentary canal, between the perspiration and the secretion of bile, between the solar plexus and the cutaneous nerves, is effective in the production of erysipelas" (Reil, *Fieberlehre*, vol. ii., 1804).

[2] Nepveu, *Des Bactéries dans l'Érysipèle*, Paris, 1870; Hueter, *Deutsche Zeitschrift für Chirurgie*, 1868, i. p. i.; *Centralblatt für die med. Wissenschaften*, 1868, No. 35.

[3] "Zur Untersuchung von pathogenen Mikro-organismen," *Mittheilungen aus dem Kais. Gesundheitsamt*, 1881, Bd. i. S. 38.

[4] Fehleisen, "Aetiologie des Erysipels," Berlin, 1883, *Verhandlungen der Würzburger med. Gesellschaft*, 1881.

ubject by ng to adhere closely to the generally admitted clinical
natomical eatures of erysipelas. By ignoring these features vari-
uthors have thought to have produced erysipelas with cultures of
nt species of micro-organisms, when in reality the change pro-
was not erysipelas at all. The idea that erysipelas in man has in
n cases been produced by other organisms than the streptococcus
hleisen (staphylococci, typhoid bacilli, etc.) has two possible sources
allacy. One of these is that the supposititious erysipelas is not a
rysipelas. This was no doubt the case with the experimental
ary erysipelas of rabbits described by Koch. The other source of
y is the fact that the organisms cultivated from erysipelatous lesions
have been recent arrivals there.

e old idea that the erysipelas cocci can be recognized by the results
noculations in animals has been almost entirely abandoned by all
ho have carefully examined the matter.[1] Whatever the future may
eveal in regard to the relation of the streptococci found in various diseases, we can at present assume that under ordinary conditions erysipelas in man is always caused by streptococci morphologically similar to the common streptococci of suppuration.

For obtaining these organisms in pure cultures various methods are used. The usual method, and the old one, is to remove a piece of affected skin with the most rigid antiseptic precaution and place it in sterilized bouillon. This is of course a method which cannot be used very frequently, and as a substitute that of Achalme[2] is preferable: After carefully disinfecting the skin a thin layer of collodion is rapidly dried over the part to be examined; a sterilized lancet is then passed rapidly through the collodion into the deep layer of the skin. The first drops of blood are removed by the aid of a sterilized pipette. The skin is then squeezed so as to press out a drop or two of serum, which is received in a sterilized pipette. From this tubes of nutrient media are inoculated. It is necessary to use a good deal of serum, because even in that from the most active seat of the disease the microbes may be rare. Cultures from different cases of erysipelas, or from the same case in different media, give results which differ slightly, as can be seen from the descriptions of various observers. On the whole, grown under similar circumstances the cultures show unmistakable resemblances.

In gelatin the colonies grown at the ordinary temperature become visible in from thirty-six to forty-eight hours. In the depths of the gelatin they appear as small, opaque, white specks, round and sharply circumscribed. Those on the surface are somewhat larger and almost hemispherical. Examined with a moderate power, the margins are seen to be slightly irregular. The centre of the colony is milk-white, the border somewhat translucent. From the fact that the gelatin is never liquefied, the streptococci can be distinguished from the white staphylococcus which may grow in the culture as the result of contamination from the skin. In agar or serum at 35° C. the colonies grow more rapidly and are more translucent.

Grown in bouillon, the medium becomes turbid in about twelve hours, but clears up in three or four days, and the cocci then form a granular sediment on the bottom.

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[1] Kurth, *Arbeiten aus dem Kais. Gesundheitsamt*, 1891, vii. 389; Von Lingelsheim, *Zeitschrift für Hygiene*, xii. 308.

[2] Achalme, "Sur l'Érysipèle," *Paris Thesis*, 1892.

In milk the streptococcus causes a local coagulation in the course of several days, followed more or less rapidly by complete coagulation and subsequent retraction of the clot, leaving the serum clear.

Examined alive in liquid, the streptococcus shows only Brownian movement.

The streptococcus of erysipelas stains readily with the usual aniline dyes, and faintly with carmine or hæmatoxylin. It is not decolorized by the methods of Gram and Weigert.

The appearance of the organism differs slightly according to the soil in which it is grown, but in general it forms short chains of from six to eight cocci on solid media. In liquid media the chains may contain as many as thirty to forty cocci. They measure from .3 to .6 micromillimetres in diameter. The chains often contain pairs in closer apposition (diplococcus forms). In old cultures the cocci show considerable variation in size, and also in intensity of staining.

The streptococcus of erysipelas grows well in the air, but it also grows anaërobically. According to Achalme, it grows better without access of air. Lubinski[1] could see no difference in the appearance of the colonies grown under both conditions. Both observers say that vitality and virulence are well preserved in anaërobic cultures. According to Achalme, the streptococcus grown anaërobically shows more marked action than otherwise, so that he claims it is really a facultative aërobe.

The streptococcus grows best in alkaline media. It produces, however, an acid reaction in the medium, which is, according to Achalme, less marked than that produced by streptococci from pus, although this observer also claims that attenuated cultures of erysipelas cocci produce an acid reaction more rapidly than virulent ones. The acidifying power varies much with the medium in which the organisms are cultivated. The nature of the acid formed is not known.

The erysipelas coccus is sensitive to extremes of heat and cold and to variations in its culture soils, but with care in the selection of the culture and the soil may be kept alive for long periods ("almost unlimited," Achalme).

Both experiments *in vitro* and clinical observations go to show that the organisms may remain latent for long periods, and then as the result of some change in the environment which favors their activity, or in consequence perhaps of the disappearance of some substance which interferes with them, they may become active. In consequence of this quality certain auto-infections may be explained.

The virulence of the streptococcus of erysipelas varies extremely—in fact, quite as much as that of the similar cocci found in other diseases. Cultures may be attenuated and their virulence restored, although the latter, or even the preservation of a fixed degree of virulence, is a matter of great difficulty.

In experimenting with cultures of erysipelas cocci, rabbits offer the best medium, and in them all the degrees of intensity of the reaction may be observed with cultures of different degrees of virulence. Thus in the most severe cases there is a general sepsis without local lesion either from inoculation in a vein or in the skin. In the descending scale of virulence we have fatal sepsis following more or less severe local lesion; localized erysipelas; mild redness and swelling of the skin. Finally, cultures may be so attenuated as to produce no local alteration.

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[1] *Centralblatt für Bakteriologie und Parasitenkunde*, Bd. xvi. No. 19, 1894.

According to numerous experiments, putrefaction is a powerful assisting source of virulence in a streptococcus culture—a fact which has an important bearing on puerperal erysipelatous infection. The symbiosis of the streptococci is doubtless of great importance. Roger made the interesting observation that injections of filtered cultures of micrococcus prodigiosus with very weak cultures of streptococcus produced a severe infection. Clinically, mixed infection of streptococcus and other bacteria is not uncommon, but so far as erysipelas is concerned reliable data are scanty.

The mode in which the organisms produce the phenomena of the disease is by no means so definitely known in the case of erysipelas as in tetanus, diphtheria, and some other diseases. Manfredi and Traversa, who were the first to experiment with soluble products of the cocci, were able to produce only transitory nervous symptoms. Achalme had a similar experience. Roger thought he obtained a soluble toxic substance from erysipelas cultures, the action of which was not in proportion to the dose employed. Roger asserted that by heating this substance at 110° C. it acquired vaccinating qualities. Courmont[1] holds that the streptococcus produces a slowly acting predisposing substance, with lasting effects, but one that acts indirectly. Brieger and Wassermann[2] found the urine in a case of erysipelas with nephritis very fatal to mice. Stern[3] found that the serum of vesicles in cases at the height of the disease was much more fatal to mice than blood serum of normal subjects.

Numerous experiments in the treatment of malignant disease by injections of erysipelas or streptococcus toxins have shown that the serums or filtrates usually produce the general symptoms of erysipelas. The experiments, however, have added little to our knowledge of the erysipelas poison.

Although the streptococcus is the cause *sine quâ non* of erysipelas, it is evident there must be other factors. First among these is individual predisposition, the real nature of which, however, we do not yet understand. That the various causes of temporary or permanent weakness of the tissues favor the occurrence of the disease we can easily believe. So alcoholism, exposure, overwork, exhausting disease, even hunger and fatigue, come in play.

A very important factor is the existence of a solution of continuity of the skin or a mucous membrane. Operations, wounds of all kinds, accidental lesions, injuries received at post-mortem examinations, acne and other skin diseases, sores or abrasions of the eye, mouth, nose, or pharynx, boring the lobe of the ear for earrings, operation wounds of the nose, throat, or mouth, cautery wounds, tracheotomy incisions, leech bites, the umbilical cord or stump, the uterus post-partum, may furnish the points of entrance of the germs. The old division of erysipelas into traumatic or surgical and non-traumatic ("idiopathic") or medical erysipelas is falling into deserved disuse, or when used at all the terms are applied in a different sense from the original one. In the old sense idiopathic cases were due to an internal alteration becoming localized in the skin, surgical cases to the entrance of a "contagium." It is reasonable to suppose in many cases that even if no wound can be seen there is nevertheless one present, however small, in the skin or a neighboring mucous membrane (throat, nose). We must, however, admit that diminished vitality of the covering epithelium may suffice for the entrance of the germ without solution of continuity, or that in certain circumstances infection may take place through physiological wounds, such as the tonsils. For such cases the term "cryptogenetic" is preferable to "medical" or "idiopathic." From what we now know of the bacteria of erysipelas we may suppose that the organisms are often present in or on the body, but lack the assisting causes necessary for the development of the process. Among these causes may be mentioned putrefaction or the presence of certain micro-organisms as already mentioned.

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[1] *Revue de Méd.*, 1890, No. 10, p. 843.

[2] *Charité Annalen*, Bd. xvii.

[3] *Congress für innere Med.*, xii. p. 286.

Disturbances of the circulation around the point of entry are important assisting causes. This has long been known to clinicians and has been demonstrated experimentally. Roger[1] found that when streptococci were inoculated into both ears of rabbits and the superior cervical ganglion of one side destroyed, the local reaction was favored on that side. He also found that section of a sensitive nerve assisted the infection. *Apropos* of this, Guinon[2] raises the interesting question whether nervous affections, such as hysterical hemianæsthesia, exophthalmic goitre, etc., have any effect on the course of erysipelas. Ochatin[3] and Von Lingelsheim[4] varied these experiments, producing hyperæmia by section of nerves, and also by the use of collodion or adhesive plaster and injecting cultures of erysipelas cocci. They found not only that the process was more severe in the hyperæmic ear, but that even cultures of mild virulence could produce severe lesions.

Filehne[5] has shown that by raising the temperature of inoculated animals the infection runs a more rapid and more favorable course.

Contagion, or the acquisition of the disease from another known case, does not occupy as important a position in regard to erysipelas as it did in the preantiseptic days. In fact, in surgical wards now the disease is hardly ever seen to spread, and when it does some error in technique can usually be discovered. It has been thought that erysipelas is contagious in the sense that it may be acquired "through the air." This is possibly only when the germs themselves are transported in that medium, and its actual occurrence is always doubtful. An interesting case of indirect contagion, which also illustrates the resistance of the organisms, is reported by Stumpf.[6] A woman had a boy infant, born in 1888. He acquired erysipelas and died. In 1889 a girl child was born and remained healthy. In 1890 another boy was born. He was washed, and the shirt worn by the first child, which had not been used in the mean time, was put on him. Thirteen days later he developed erysipelas, with a relapse and ultimate recovery.

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[1] *Comptes rendus de la Société de Biologie*, 1890, p. 222.

[2] *Traité de Médecine*, tome ii.

[3] *Arch. de Méd. expér. et d'Anat. path.*, iv. 2.

[4] *Zeitschrift für Hygiene*, xii.

[5] *Proc. Physiolog. Soc.*, *Cambridge*, Aug. 11, 1894.

[6] *Deutsche med. Woch.*, March 17, 1892, p. 231.

Erysipelas is influenced to a certain extent by atmospheric conditions. In this country it is most frequent in the early spring. Low temperature and moisture and rapid changes in temperature aid in its production. According to the investigations of Anders,[1] the number of cases increases from August to April (in Philadelphia), and then decreases. One half of all the cases occur in February, March, April, and May. These relations are not always the same in other places and times.

Erysipelas is most frequently observed in early middle life.

Notwithstanding the greater exposure to wounds on the part of men, the temporary predisposition furnished by the puerperal condition makes the relative proportion of the sexes less unequal than might be supposed. Anders puts the proportion of men and women affected as three to two.

PATHOLOGICAL ANATOMY.—Even during life the lesion of erysipelas exhibits the cardinal signs of inflammation. After death the redness and swelling are diminished, especially the former. The microscopic alterations in the tissues have been carefully studied in pieces excised during life, controlled by the examination of experimental lesions in animals. Our knowledge of the changes is due largely to the investigations of Vulpian, Volkmann and Steudener, Renaut, Tillmanns, Ranvier, Cornil, and others, though the researches of Fehleisen have thrown a light on them which former investigators could not give. Recently Unna has published the results of his observations, which fill out important lacunæ. Following Fehleisen, the lesions are described as in three zones. The outer zone is beyond the raised margin of the erysipelatous area. Microscopically, this zone shows masses of cocci in the lymph spaces, but no alterations in the tissues. This zone passes into the middle one, corresponding to the advancing margin of inflammation. It is characterized by the evidences of inflammatory reaction in the tissues.[2] The vicinity of the streptococcus colonies contains numerous small cells, and some of these cells contain cocci. In the third zone cocci are few or absent, but there are traces of inflammation in the stage of retrogression or absorption. According to Unna,[3] the process affects the skin and subcutaneous tissue simultaneously, but heals more rapidly in the skin, and seldom reaches the height it does in the deeper tissue. In the subcutaneous tissue he finds that the cocci are not confined so especially to the outer zone as in the skin—a difference which he suggests is due to more favorable conditions for the growth of the cocci in the deeper tissue. This corresponds to a more severe process in the subcutaneous tissue.

In the inflammatory areas vascular changes are marked. The veins and capillaries are distended with blood. The leucocytes are not arranged especially along the walls of the vessels, but often form small groups in the vessels. They are distinctly increased in these parts. The capillaries often contain rows of leucocytes, though according to Unna diapedesis is not a constant occurrence. The arteries are dilated in some places, and besides an increased proportion of leucocytes contain much coagulated fibrin. In other places the arteries are narrow, but plugged with fibrinous thrombi, containing leucocytes. In some of the veins central thrombi are to be seen, evidently propagated from those in the arteries or capillaries. There is, then, a paralysis of the vessels, especially of the veins, with slowing of the current, adhesion of leucocytes, and intravascular formation of fibrin, especially in the arteries.

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[1] *Journal of the American Medical Association*, July 22, 1893.

[2] In erysipelas lymphangitis is part of the process, yet lymphangitis and erysipelas are not identical, either clinically, anatomically, or etiologically. Lymphangitis may be produced by various kinds of bacteria, as shown by the researches of Fischer and Levy (*Deutsches Archiv für Chirurgie*, xxxvi., 1893, H. 4 u. 5).

[3] *Histopathologie der Hautkrankheiten*, Berlin, 1894.

The lymph spaces and lymph vessels are distended with lymph containing streptococci in chains and masses. The leucocytes are found in greater numbers as the process advances. In many places in the lymph vessels there are firm white thrombi.

The vascular changes are by no means the only ones of importance. The connective tissue breaks down and liquefies, or becomes fibrillated or converted into a pulpy mass. The elastic tissue degenerates. The spindle cells of the skin break down and their nuclei disappear. The striped and smooth muscular fibres of the skin undergo a fate similar to the other tissues.

The epithelial tissues suffer also. The swelling of the papillæ loosens their connection with the overlying tissue. When the papillæ break down the epithelium follows, the nuclei lose their staining capacity, the protoplasm becomes indistinct and stains less readily. According to Unna, the epithelial cells do not swell, but the degenerated and partly necrotic epithelium is raised *in toto* from the papillary layer, forming thus blebs or vesicles. In the contents of the vesicles cocci are rare in the beginning, but fibrin and leucocytes are always present. Later, bacteria of various kinds can be found in the vesicles. Sometimes the leucocytes are so abundant in the contents of the vesicles that the liquid is turbid or opaque, or, in other words, purulent. Occasionally vesicular degeneration of the epithelial cells takes place, as described by Cornil, but this is not the cause of the gross vesicular lesions, which are due to the œdematous infiltration of the papillary layer of the skin already described.

In contrast to the marked changes in the surface epithelium, that of the sweat glands and hair follicles is often little or not at all affected. In severe cases the hair follicles undergo changes similar to those in the surface epithelium.

Erysipelatous inflammation of the skin may be described as a serofibrinous inflammation, but it may and sometimes does pass on into a suppurative or necrotic form.

In the deep tissues erysipelas causes changes of a different kind, especially when the subcutaneous tissues are well developed. The lymph vessels and lymph spaces in the coats of the large vessels in the septa of the adipose tissue form the paths of the cocci, which are present in these parts in enormous numbers. Usually the cocci do not penetrate farther than the adventitiæ of the vessels. The vessels themselves do not contain thrombi, as do those in the skin, but the fat lobules and their capillaries contain large masses of fibrin. There are also large numbers of leucocytes which break down, forming pus in the septa of the fat tissue. This process often extends deep into the muscular tissue.

The process in the deeper tissue is therefore a fibrino-purulent inflammation, although not recognizable clinically as purulent. In fact, in the majority of cases which seem to be superficial the deep-lying pus is absorbed without being discovered. It is when the pus makes itself known clinically that the term phlegmonous may be applied. (In addition to this there is, of course, occasional phlegmon formation as the result of a complication to be mentioned later.)

In the healing of erysipelas the cocci die, and they as well as the leucocytes and thrombi are removed from the areas in which they were. As blood begins to flow through the vessels the epithelium is renewed, forming a layer which desquamates at first, but ultimately becomes permanent. Finally the muscles, connective tissue, and elastic fibres are regenerated.

As is well known, erysipelas is one of the diseases in which Metchnikoff asserted the importance of phagocytosis. Perhaps most investigators, however, consider that in erysipelas phagocytism in the manner originally described by Metchnikoff is not so important as the latter claimed. That the leucocytes frequently contain cocci, in different stages of degeneration very often, is admitted, but the general belief is that the cocci have been seriously affected before becoming the prey of the phagocytes. In the healing of erysipelas macrophages, containing leucocytes, fibrin, cocci, and unrecognizable débris, can be seen.

The earliest claims to the discovery of germs of erysipelas include accounts of bacteria in the blood. Later observers are unanimous in holding that as a general thing the cocci do not enter the blood circulation, notwithstanding the fact that they are frequently carried considerable distances in the lymph vessels. Even if they enter the blood by way of the lymphatics, they must do so so rarely and in such small numbers that they are disposed of in the blood without setting up other processes.

That the cocci can, and in rare cases do, enter the general circulation was shown first by the observations of Von Noorden and Pfuhl. Sudakow[1] examined 5 cases of erysipelas with reference to this point. He found cocci in 2 cases in both blood and sweat. In one case the blood, in another the sweat only, contained the organisms. Achalme[2] was unable to cultivate organisms from large quantities of blood in 18 cases of erysipelas of moderate severity. On the other hand, in 3 fatal cases he was able to cultivate them from the blood (in the heart), and in 2 cases he found cocci in the urine.

The probability of the cocci setting up metastatic processes by way of the blood depends partly on their virulence, partly no doubt on the numerous accidents to which they become exposed when they leave the lymph spaces, in the plasma or in the bodies of the leucocytes, and are carried toward the blood circulation. Here they are either disposed of or, under favorable circumstances, produce lesions which will be considered under Complications (p. 467). A diminution of the red blood corpuscles in the active stage of the disease was noticed by early investigators in that field, but does not seem to be constant. An increase of leucocytes, especially the polynuclear neutrophile cells, amounting to as much as two or three times the normal, is perhaps a constant occurrence. An increase of fibrin has been observed by many since it was first noticed by Andral and Gavarret.

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[1] *Centralblatt für Bakteriologie u. Parasitenkunde*, 1893, ii. p. 817.

[2] *Loc. cit.*, p. 236.

Inflammation of the regionary lymphatic vessels and glands occurs in the course of erysipelas as part of the disease, but is marked only in cases of unusual severity or as a complication. Occasionally lymph glands some distance from the skin lesion are affected, sometimes very early in the disease. Other anatomical alterations play a subordinate part in erysipelas, and will be considered under the head of Complications (p. 467).

SYMPTOMS.—The stage of incubation of erysipelas is either without symptoms or has those common to many other infectious diseases—malaise, anorexia, lassitude; in some cases an indefinite feeling of exhilaration, perhaps from slight fever, can sometimes be recalled by the patient. The duration of this stage is variable. According to observations of Widal and Netter and of Echalier[1] in patients who acquired erysipelas by exposure to other known cases the incubation was respectively two, six, ten, thirteen, and fourteen days. In Fehleisen's experiments on men the duration varied from fifteen to seventy-two hours, which corresponds to the period usual in animal inoculations (one to three days). Cases without a discoverable wound sometimes seem to have a longer period of incubation than others.

The first striking symptom, which is rarely absent, is a chill. Usually the chill is sudden and severe, resembling the chill of malarial intermittent fever or of croupous pneumonia or the severe chills of septic infection, to which, indeed, the erysipelatous chill has a close affinity. It may last for only a few minutes or from one to two hours. The usual duration of the chill is less than half an hour, with cold skin, cyanosis of the lips and extremities, chattering of the teeth, and trembling. From the severity and the duration of the chill an idea of the severity of the disease may be formed.

During the chill nausea and vomiting usually occur. The vomitus is not peculiar, but when vomiting is severe bile is often present, and so keeps up the tendency to perpetuate the term "bilious erysipelas."

After the chill, or sometimes shortly before it, the temperature rises, usually rapidly, reaching 102° F. or more according to the severity of the case. The pulse is frequent in proportion to the rise of temperature, but full and strong. Nausea and a feeling of discomfort in the epigastrium, with loss of appetite, continue. The tongue is slightly swollen, with a yellow coat. There is continued malaise. Headache is a common symptom. With some or all of these symptoms a day or more may elapse before the disease in the skin becomes visible. It was this period between the appearance of the general symptoms and those in the skin that seemed so convincing of the dyscrasic nature of the disease at a time when the nature of infection was so much less understood than it is now.

During this period the diagnosis is usually in doubt, or if there are marked cerebral symptoms the case may be considered one of typhoid

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[1] *Paris Thesis*, 1890.

Occasionally careful examination or the patient's own account
es tenderness or swelling of the lymphatic glands supplied by the
ffected. In some cases tenderness of the lymphatics, less fre-
swelling, precedes the inflammation of the skin by several days.
s beginning in the nose epistaxis often occurs, either spontan-
or from blowing the nose.

ore the inflammation appears the patient almost always has a
on of fulness or tension, sometimes a prickling or itching in the
ffected. When the infection takes place in the nose there may be
usual sense of fulness and pain, beginning very soon after the
nd followed by the usual symptoms of coryza. When the inflam-
begins in a visible wound the latter sometimes becomes paler
the special process appears.

characteristic erysipelatous lesion varies in color from a yellow-
to a bright or deep red color. In anæmic or cachectic persons
r is paler. Pressure causes the color to pale, showing a yellow-
in the anæmic parts, but it immediately resumes its previous
when the pressure is removed. The surface of the skin is usually
ing, but finely or coarsely granular according to the texture of the skin in the part affected. The appearance of the surface has been well compared to that of an orange. The characteristic feature of the erysipelatous patch is abrupt margin by which it is sharply marked off from the sound skin. The distinctness of the margin and the elevation of the inflamed surface vary in different cases, depending partly on the thickness of the skin. The margin sometimes is regular, sometimes zig-
ag, and again not at all distinct. This is especially so when erysipelas
ffects skin previously the seat of an ordinary inflammation or skin which is rugous, as that of the scrotum. Sometimes the margin can be recognized more easily by touch than by sight. An additional aid to its detection is that by examining the affected area through a glass plate with pressure. This method of examination, "diascopy" of Unna,[1] can be practised with a microscopic slide or a watch-glass, or by the more complicated method of Liebreich, called by him "phaneroscopy."

The affected skin feels hard, brawny, like congealed skin or that of a cadaver. It cannot be pinched up in a fold except with difficulty. Pressure increases the pain. The inflamed part not only gives the subjective sensation of heat, but is actually warmer than the normal skin.

On the surface of the inflamed area, except in the mildest cases, vesicles or bullæ appear as the process reaches its height. By coalescing these form large areas more or less elevated, filled with a fluid which is at first clear, later turbid. The epidermis over the vesicles easily becomes broken, and the serum, often mixed with blood or pus, dries on the surface.

The erysipelatous patch enlarges by spreading in waves or irregular lines, "like an oil drop on paper." The extension is rarely symmetrical or even on all sides, but may spread on one side while remaining stationary or receding on others. The spreading takes place by stages. Sometimes it can be seen that the process is arrested temporarily where the skin is firmly attached to the deep tissues, as at the naso-labial fold, the margin of the hairy scalp, Poupart's ligament, etc.

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[1] Unna, *Berliner klin. Wochenschr.*, No. 42, 1893.

The swelling involves not only the skin, but also the subcutaneous tissue, thus adding greatly to the deformity. The process is greatest where the skin is loosely attached, as in the eyelids, lips, scrotum, and external genitals. The œdematous swelling in these parts adds much to the distortion characteristic of the disease.

The temperature, which rises rapidly after the chill, reaching a height of 104° or 105°, remains elevated as long as the inflammatory process is active. The temperature is usually remittent, with a morning fall of one or more degrees. Usually the remissions are more marked in mild or favorable cases, and in these the temperature may be intermittent. (This has no necessary relationship with malarial infection, though it was formerly looked on as showing a malarial origin of the disease.) On the other hand, very severe cases may show marked remissions, as in one under my observation in which the temperature showed a daily difference on successive days of 3°, 3.4°, 5°, 5.5°, 4.2°, 4.6° F. Complications, especially internal complications, have a tendency to increase the temperature, and relapses are almost always preceded by a sudden rise. If death occurs in hyperpyrexia, the temperature sometimes continues to rise post-mortem. In rare cases, sometimes otherwise severe, there is no elevation of temperature at all—*afebrile erysipelas*.

The pulse follows the course of the temperature during the height of the disease, with certain limitations. In cachectic persons it is relatively frequent. In cases with jaundice it has been observed to be relatively slow.

The other symptoms are usually severe in proportion to the eruption and fever. Prostration, loss of appetite, coated tongue, and constipation are almost always present. In severe cases delirium is common, usually of a mild kind. In others there is apathy, stupor, or even coma. In the most severe cases the typhoid condition comes on, with sordes on the lips and tongue—the latter being dry—trembling, delirium and sometimes convulsions or coma.

The urine usually contains albumin, hyaline casts, and increased numbers of leucocytes, and sometimes red corpuscles and renal epithelium.

At the height of the disease the local symptoms are marked. As the redness and swelling invade new areas, with their characteristic subjective sensations of intolerable tension and itching, the parts earlier affected become pale and less tense, although subcutaneous inflammation and œdema cause the swelling to remain for some time. The duration of the swelling and redness in any one part varies much in different cases. Sometimes the whole process is over in a few hours; again, it may take a week or more to reach the stage of resolution, even without complications.

In recovery the swelling subsides, the temperature falls, the pulse often becomes abnormally infrequent. The gastric symptoms subside, appetite improves, and convalescence is usually rapid in uncomplicated cases. The fall of temperature often precedes the other symptoms of recovery. It is usually rapid and marked in cases which recover promptly, slow or irregular in others. Yet there are exceptions to this, and severe relapses or complications sometimes follow in cases with marked crises. The losses of epidermis from vesicles, scratching, or ment are restored. Desquamation, usually in fine scales, sometimes tches, continues for some time. The affected skin, especially that e nose and face, often remains hyperæmic for a long time. The falls out when the scalp has been affected, but soon grows again. new hair is apt to be curled or darker than before, but soon resumes former appearance. In parts where the skin is loose, as in the eye-s, œdema is likely to persist for some time.

Recurrences.—Erysipelas is one of the acute diseases in which recur-ce takes place—a fact which gave much trouble to those who sup-ed that infection always produced immunity, but at the same time shed to include erysipelas among the exanthemata. Relapses may cur in convalescence, beginning in the same point as the original dis-se or elsewhere. They are usually not so severe nor of as long dura-on as the primary attack, but they do not always become successively milder, as has been supposed. Attacks occurring after long intervals are also likely to be less severe than the first one, thus giving support to the idea that a sort of immunity is produced, but to this, too, there are exceptions.

Some individuals seem extremely disposed to recurring erysipelas, as in the subjects of so-called menstrual erysipelas, first described by Hoffmann in the last century. Hirtz and Widal[1] have reported the case of a woman of fifty who had erysipelas every month at the time the menses had usually occurred. As an example of the number of recurrences which can take place, the same observers report the case of a woman who for four years was free from the disease only two months. Admitted to hospital for nephritis, she had in the next three months twenty distinct attacks of erysipelas on the face and thighs. The latter began in a chronic eczema. Some of the attacks were afebrile; in one the temperature was above 40.5° C. for a week. The blood contained virulent streptococci in both mild and severe attacks. Critzman[2] reports the case of a woman who from the age of thirty to thirty-five had erysipelas almost regularly at the time of menstruation. A piece of excised skin in one attack showed streptococci of Fehleisen.

Recurrences may be explained by a retention of the germs in the body in a latent form, which, according to experiments *in vitro*, may last for long periods. The following observations show a not infrequent mode of recurring erysipelas: A man with an old wound of the right orbit was admitted to my wards with severe angina. On the fourth day, when the angina had subsided and the temperature reached 99° F., the patient had a chill, with a rise of temperature, soon followed by severe erysipelas of the face, beginning around the orbital wound. The temperature reached 105° F. every day for four days, notwithstanding full doses of salol, and then fell slowly with disappearance of the erysipelas. A purulent discharge from the right frontal sinus was treated locally in the eye ward. Two days after complete disappearance erysipelas began again, but subsided rapidly under the use of ichthyol. Six days later another attack came on, beginning, as had the others, at the wound. This attack was quite severe and lasted a week. Ichthyol was used as before. I then had an opening made into the left frontal sinus, with permanent drainage and thorough irrigation, and the patient made a complete recovery.

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[1] *La Bulletin médicale*, 1891, No. 101, p. 1163.

[2] *Arch. gén. de Méd.*, 1892, Jan., p. 24.

Variations in the Course of the Local Lesion.—The erysipelatous lesion varies much in its course, appearance, and intensity in different cases. Various terms have been applied to those varieties, most of which suffer from having been used in different senses by different writers. I shall mention only the commonest.

The term *fixed* erysipelas is given by some writers to mild cases which remain localized in the vicinity of the point of origin. Others apply the same term to an inflammation which occurs especially around chronic ulcers. This latter is not, as a rule, identical with true erysipelas.

Migrating, ambulant, or wandering erysipelas is spoken of when the disease tends to spread by continuity from the point of origin in one or more directions. This is the typical course of the disease, but, as the extent varies greatly, some writers apply the term only when the disease affects large territories, receding at one end while it advances at the other. The progress of the disease sometimes follows definite lymphatic paths, but often no such course can be recognized. Sometimes it follows the lines, called Langer's, of the minute fissures of the epidermis.

Erratic erysipelas is a term given by many to a form resembling the one just described, but differing in the fact that the areas are not continuous. Sometimes several foci develop about the same time. This has also been called *multiple* erysipelas. Both this and the preceding form may affect parts in which the eruption has wholly or partly subsided.

Erysipelas is sometimes called *serpiginous* when the lesion is both extensive and irregular.

Variations in the Character of the Local Lesion.—Erysipelas varies in intensity from a slight redness and swelling in the outer layers of the skin to the most severe inflammatory affection. Besides these degrees there are certain varieties which need mention. In many cases the names given to these are superfluous, although sometimes convenient in practice.

Œdematous erysipelas is spoken of when œdema is a predominant feature. This is almost always the case in certain parts of the body, as the scrotum and the eyelids. It is also likely to be marked in the subjects of heart or kidney disease. In phlegmonous and gangrenous erysipelas œdema usually appears early.

Bullous or *pemphigoid* erysipelas only differs from the ordinary form in the greater size of the vesicular lesions, which occur in all but the mildest cases.

Under the old term *white* erysipelas, formerly applied to the œdematous variety, Achalme describes a case in which all the symptoms and signs of erysipelas were present but redness. Streptococci were found in great numbers in the deep lymphatics. Notwithstanding Achalme's remarks, it seems that such cases have more resemblance to lymphangitis than to erysipelas, although the distinction is not a very important one.

Hemorrhages, usually of small size, occur in most cases of severe erysipelas. In some cases they are so marked as to lead to the use of the term *petechial, hemorrhagic*, or *ecchymotic*. Extensive hemorrhages occur especially in cachectic persons and are of bad prognostic import.

Juhel-Rénoy[1] gave the name *érysipèle à type petechial couperosique* to ertain cases which are always severe and frequently fatal.

In the section on Pathological Anatomy (page 456) the fact was mentioned that in every severe erysipelas suppuration occurs. In most ases suppuration or phlegmon formation in the ordinary clinical sense does not occur. In some cases suppuration becomes manifest in different degrees, so that circumscribed phlegmon or abscess, diffuse phlegmon, or purulent œdema can be distinguished. These all fall under the name *phlegmonous* erysipelas. Although these processes can be produced by the intensity of the action of the erysipelas coccus, they may be, and metimes are, due to mixed infection with some other pyogenic germ. ke other suppurative diseases, they are less frequent now than formerly.

The phlegmonous complication usually develops in the end of the st or beginning of the second week. Sometimes it develops slowly without marked local signs; again, the skin becomes more indurated nd darker, the pain is more severe, the lymphatic vessels in the vicinity are red and hard, the parts feel full. Often there are repeated chills, with increase of fever, nausea, and vomiting, and increased prostration. As the process continues the pain becomes less severe, but the general symptoms are more marked, and usually the common signs of sepsis are present, including, in severe cases, the typhoid state. The abscesses may open spontaneously, but frequently this is delayed, so that when an opening does occur the quantity of pus, sloughs, and débris evacuated is usually large. The number of abscess foci may be large, as many as sixty-nine having been counted in a patient who recovered.

Gangrenous erysipelas often develops with the phlegmonous variety or appears as a terminal phenomenon in it. In some cases it is no doubt due to secondary infections, but it is of most importance when it occurs especially as a primary affection in old persons, drunkards, or persons with atheroma, diabetes, or chronic nephritis. Gangrenous erysipelas occurs most frequently where the skin is loose, as on the eyelids, scrotum, and labia. In such cases the skin soon becomes dusky; the vesicles which form contain reddish serum which soon dries, turning brown or black. The epidermis itself often becomes black and dry. The swelling and induration are often not marked. Usually sloughs of various sizes form in all parts of the affected skin. In a few days these separate, leaving ulcers with necrotic surfaces. In gangrenous erysipelas general symptoms are severe. The typhoid condition is almost always present, the pulse weak and irregular. Death usually occurs in a few days.

The typhoid condition is not an unusual feature in severe erysipelas, so that the attempt to make a special form of the disease, *typhoid* erysipelas, is not warranted. The presence of the symptoms making up that condition is not necessarily of fatal augury.

The term *bilious* erysipelas has been handed down from a time when bile played a more important part in the causation of disease than it does now, and sometimes the bilious vomiting of the early stages leads to the application of the term. It should be used, if at all, for those cases in which there is a marked "bilious" condition, with epigastric pain, constipation, or diarrhœa, an icteric hue of the skin and scleræ, and bile coloring matter in the urine. This depends on an intoxication or an inflammation involving the bile ducts. It is important to distinguish this from cases of erysipelas complicated by general sepsis, in which the jaundice is due partly at least to destruction of red blood corpuscles.

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[1] *Archives gén. de Méd.*, Jan., 1894.

Erysipelas of Special Regions.—*The Face.*—The commonest and at the same time the most important seat of erysipelas is the face. This is true especially of "medical" erysipelas. The predilection is readily explained by the greater exposure to wounds and also to the micro-organisms. Corresponding to the most common seat of inoculation, the local lesion usually appears first in or on the nose, from which it spreads in different directions, and often so symmetrically that at a certain stage the area of inflammation has a shape somewhat resembling that of a butterfly with the wings spread. In mild cases it extends no farther than the middle of the cheeks and is limited to the skin. In other cases the disease passes down to the angles of the jaws, up to the scalp, and back to the ears. Often the progress is temporarily arrested where the skin is firmly attached to the deep tissues, as at the naso-labial fold and the margin of the hairy scalp. For a similar reason the chin is seldom affected as severely as other parts of the face. In all but the mildest cases the subcutaneous tissues are also affected. The eyelids soon become swollen, and so thickened that they cannot be opened. The nose is broad and shapeless; the lips are swollen and their motion painful; the ears form large swollen masses; the nares are occluded; the mouth and tongue are dry; the tongue is red or brown, sometimes fissured and bleeding. In other cases the inflammation passes down the neck and surrounds it. In such cases the scalp is usually invaded from different directions. This is accompanied by the most severe pain, although, owing to its texture, the swelling is not so great as in other parts of the body. From the swelling of the skin, aided by that of the deep tissue, the vesiculation and scabbing, the swelling of the eyelids, between which purulent secretions trickle, the swelling of the nares, causing the patient to breathe through the thickened lips, the aspect of the patient is most repulsive. When the scalp is invaded the symptoms usually reach their acme. All the general symptoms of the disease are present, and headache, restlessness, and delirium are rarely absent. The nervous symptoms are often so severe that meningitis is suspected. Formerly, in fact, it was thought that the inflammation often passed down the veins into the cranial cavity, but this rarely happens. The nervous symptoms are readily explained on the ground of intoxication, as held by Todd long ago, or fever, and are often as serious even when the scalp is not involved or when the local disease is at the opposite end of the body.

The duration of erysipelas of the face varies as that in other parts, from a day to one or two weeks, usually lasting about a week.

Erysipelas of the body and extremities occurs most frequently as a complication of surgical diseases. It does not require special consideration, as the general and local symptoms are similar to those already described.

Erysipelas of the Mucous Membranes.—Erysipelas affecting the mucous surfaces is sometimes called *internal* erysipelas. In these parts the disease may be primary or secondary. As the structure of many of the mucous membranes resembles closely that of the skin, it may be admitted that they offer favorable localities for the activity of the erysipelas coccus, but the real nature of many so-called primary cases of erysipelas of the mucous membranes may be questioned.

The Nose, Mouth, and Pharynx.—Judging from the frequency with which erysipelas first appears on the nose, it would seem that the nasal mucous membrane is often the starting point of the disease. This is no doubt true, and yet it must be remembered that the infection may take place in the nose without setting up the characteristic lesion at the point of entrance, just as infection may take place in a wound in the outer skin and the disease begin some distance from it. The disease usually begins like a coryza, with dryness followed by increased secretion, and is soon attended by unusual pain and the other symptoms of erysipelas. Very often erysipelas begins during an ordinary attack of coryza, the latter furnishing the necessary conditions, and the first suspicion of the existence of more severe disease is caused by the chill, followed by the other general, and finally the local, symptoms of erysipelas.

The occurrence of erysipelas of the pharynx has been observed for a long time as an isolated affection and in epidemic form. It is usually supposed that the "black tongue" which attracted so much attention during the middle of this century was erysipelas. It seems much more likely that these were for the most part cases of diphtheria, possibly streptococcus diphtheria.

Erysipelas of the pharynx, including the tonsils, may be primary or secondary. Infection may take place in the latter by way of the mouth, nose, and lachrymal ducts, or even by the ear. In any case the diagnosis can only be made when erysipelas appears on the skin. Without that the most accurate term that could be given (in case of bacteriological examination) would be streptococcus angina.

The local symptoms are those of an angina, varying from a mild catarrhal to a diphtheritic, phlegmonous, or gangrenous inflammation. Generally the lymphatic glands at the angle of the jaws are unusually swollen and tender. The other symptoms are those of erysipelas in other locations, but, as remarked above, it is only when cutaneous erysipelas is present that the diagnosis can be made. In any event, the throat affection should be treated as an angina after its kind in each case.

Erysipelas of the mouth is much rarer than that of the pharynx. It is usually secondary and requires no special description. The stomatitis which develops in many cases of erysipelas hardly deserves the specific term.

Chantemesse and Widal claim that inflammation of the submaxillary glands (angina of Ludwig) is of erysipelatous origin, having found streptococci in the exudate in that condition. I have seen Ludwig's angina as a complication of erysipelas.

The Larynx.—Erysipelas of the larynx, which was described long ago by English physicians, may be primary or secondary. The latter is recognized by the appearance of the lesion elsewhere. The former is of more importance on account of the belief that many cases of so-called idiopathic œdema of the glottis are erysipelatous. It is also thought that many cases of phlegmon of the larynx are erysipelatous. Massei[1] and Delavan[1] deserve credit for calling attention to the subject. Virchow soon after predicted that many acute cases of œdema of the glottis would prove to be erysipelatous, as the anatomical conditions in both diseases are similar. Biondi and others have found streptococci which could not be distinguished from those of Fehleisen. The question of nosology need not be discussed here. Massei gives the following distinguishing features of the disease: Marked swelling of the mucous membrane, developing almost constantly in the glandular tissue at the base of the tongue, soon spreading to the epiglottis and aryepiglottic folds; rapid passage of the swelling from one part to the other, with sudden appearance and disappearance of dyspnœa; high fever in the beginning. Herzfeld[2] calls attention to the phlyctenæ on the epiglottis, some of which disappear, while others break down and form superficial ulcers. This condition, which Massei also describes, was noticed by Gottstein in primary œdema of the larynx. Herzfeld thinks these spots are due to a mild subepithelial exudate, and are not true vesicles. Pain in the prelaryngeal region is a marked symptom. Massei ascribes it to inflammation of the prelaryngeal ganglia.

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[1] *Das primäre Erysipel des Kehlkopfs*, German translation by Vincenz Meyer, 1886.

Erysipelas of the lower respiratory passages, the lungs, and pleura are important chiefly as complications. Many cases described under that name have been cases of streptococcus infection which are not definitely entitled to the term erysipelas.

The Genital Mucous Membranes.—Although admitted as possible by some writers, erysipelas of the urethra of man must be exceedingly rare. Achalme could not cultivate the specific organisms in normal urine even when made alkaline, and obtained no results from the injection of one c.c. of a virulent culture in the bladders of rabbits.

In the female, on the contrary, erysipelas of the genitals is of great importance on account of its association with the puerperal state. As this subject does not belong to internal medicine, it cannot be further considered here.

Transmission of Erysipelas from the Mother to the Fœtus.—The possibility of this, which has no doubt occurred, depends on the circulation of the germs in the blood, a matter which has been mentioned in an earlier part of this article. Although abortion is not rare in pregnant women with erysipelas, such patients rarely have pyæmia, which would almost necessarily follow in case the organisms could reach the fœtus in a virulent condition. The abortion must therefore be due to other causes than fœtal erysipelas.

Erysipelas of the newborn occasionally occurs by infection of the cord or stump, and begins on the abdominal wall. It also occurs in the newborn, as in later life, in accidental wounds, excoriations (nose, vulva in intertrigo), and skin diseases. It sometimes complicates circumcision when performed without aseptic precautions. Many cases of so-called erysipelas of the newborn are really cases of sepsis, usually produced by streptococci, but often complicated by other organisms.

COMPLICATIONS AND SEQUELÆ.—The complications of erysipelas are due either to unusual localization, or to unusual severity of the essential disease, or to secondary infections. Many of them are almost constant, and might be considered as ordinary phenomena of the disease; such is albuminuria. Others are rare.

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[1] *New York Medical Journal*, Sept. 12, 1885, p. 284.

[2] *Arch. für path. Anat.*, Bd. 133, p. 176.

Erysipelas affecting the eyelids is sometimes followed by suppurative conjunctivitis, keratitis, iritis, detachment of the retina, and even destruction of the bulb. Glaucoma has been observed as a late sequel. In other cases inflammation affects the orbital connective tissue and produces exophthalmos, thrombosis of the sinuses, infection of the meninges, or, as a late complication, optic atrophy.

The ear complications of erysipelas have been well described by Haug.[1] The affection is usually secondary. Primary erysipelas of the ear has followed boring the ear, itching diseases of the ear, or removal of impacted cerumen. Usually the internal ear is not affected, except by temporary hyperæmia. In the external canal erysipelas causes swelling, with vesicles. Necrosis does not often occur, but suppuration sometimes does. Eczema may follow. Usually the disease does not pass the tympanic membrane, but in severe cases otitis media occurs, and even abscess of the mastoid antrum. Sometimes suppuration of the mastoid cells occurs without perforation of the tympanic membrane. Erysipelas rarely affects the ear by extension from the pharynx.

Parotitis occurs in some cases in which the mouth or pharynx has been involved. It frequently goes on to suppuration.

Empyema of the antrum of Highmore occasionally follows erysipelas of the face.

The coated tongue, vomiting, and other evidences of gastric disorder so common in erysipelas are usually explicable by the intoxication and fever. In rare cases inflammation, exudation, and ulceration of the mucous membrane of the duodenum occur, with streptococci in the lesions examined post-mortem. In other cases diarrhœa with bloody stools has been observed, leading to the supposition of an erysipelatous enteritis. In many cases it is probable the enteritis is septic, not necessarily due to specific organisms. Rendu has reported an interesting case in which facial erysipelas spread into the mouth and pharynx, and after several days, during which the patient had severe gastro-intestinal symptoms, appeared at the anus.

Ucke[2] has reported a case of secondary erysipelas of the stomach.

Erysipelas is a comparatively common complication of wounds and ulcers in or near the anus.

The liver is often enlarged, the seat of parenchymatous degeneration and sometimes of necrotic foci.

The spleen undergoes similar changes, and an enlargement of that organ has been looked on as an important diagnostic sign. Frequently, however, the spleen cannot be felt.

Albuminuria is an almost constant symptom in erysipelas, occurring in about two thirds of cases of all degrees of severity. Usually the albuminuria lasts but a short time in the height of the disease, and the amount of albumin is small. Hyaline casts, an increased number of colorless corpuscles, and red blood corpuscles occur at times in the urine even in mild cases. Usually the lesion causing these symptoms is due to intoxication, but some observers have found organisms in the urine similar to those in the skin. In rare cases nephritis occurs, with large quantities of albumin, epithelial and blood casts, and free blood corpuscles in considerable numbers. Salinger[1] has seen uræmia in such a case. Various lesions, such as diffuse nephritis, glomerulo-nephritis, and septic interstitial nephritis, have been observed. As a general thing, the nephritis of erysipelas does not become chronic. Nephritis is sometimes absent in the most severe cases of erysipelas.

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[1] *Prager medicinische Wochenschrift*, 1893, No. 37.

[2] *Centralblatt für allg. Path. und path. Anat.*, p. 473, 1894.

Pericarditis is comparatively rarely observed, though no doubt sometimes overlooked, as it is in other diseases. It has been observed in different forms, from pericarditis without effusion to suppurative inflammation with streptococci in the exudate.

Endocarditis is much more frequent, and usually occurs in the later stages of the disease. It usually affects the mitral valve. The symptoms, physical signs, and outcome of erysipelatous endocarditis are like those of other cases of infective endocarditis. Accidental systolic murmurs are comparatively frequent.

Myocarditis has been observed in erysipelas as in other infectious diseases. The changes are both proliferative and degenerative.

Endarteritis and degeneration of the intima and media of the arteries have an importance chiefly anatomical.

Pleurisy and pneumonia are rare complications of erysipelas, found most frequently in cases with general sepsis. Cases of pneumonia in which the local lesion seemed to vary during life, and in which the lesions post-mortem were irregular or serpiginous, have been called erysipelatous. The peculiarities mentioned, however, do not demonstrate the specific nature of the cases, as they are sometimes present in true croupous pneumonia, and there is no advantage in applying the term erysipelatous unless the clinical relationship is evident, and very little even in that case.

Peritonitis occurs very rarely, either as part of general infection or by extension from the female genitals.

Inflammation of the meninges or brain is rare in erysipelas. Occasionally the former occurs from the extension of inflammation from the orbit or along one of the cranial nerves. It is sometimes due to organisms other than the specific streptococcus.

Peripheral neuritis is a very rare complication.

Various affections of the joints occur in erysipelas. When the skin is involved over a joint an effusion in the latter sometimes occurs from the extension of inflammation to the serous membrane of the joint. Sometimes this serous effusion seems to be due to obstruction of the lymph circulation. In other cases suppuration takes place in the joint as part of a general septic condition. Occasionally there is a monarthritis from the localization of micro-organisms in a single joint. In some of these cases pure cultures of streptococci have been found. In an interesting case observed by Galliard,[2] in which the right knee became inflamed on the sixth day of a facial erysipelas, the pus in the joint contained both staphylococci and streptococci. As a rare occurrence multiple arthritis with the characteristics of acute rheumatism has been observed.

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[1] *Medical News*, July 4, 1891.

[2] *Centralblatt für Bakteriologie und Parasitenkunde*, 1893, ii. p. 436.

Serous effusions and inflammations take place sometimes in the sheaths of tendons.

One of the late sequels of erysipelas, especially that of the face and scalp, is seborrhœa. A not uncommon consequence of repeated attacks of erysipelas is chronic dermatitis. In some of these cases a chronic hyperplasia of the subcutaneous tissue takes place, with dilatations of lymphatics, which is spoken of as elephantiasis. As a rare sequel of recurrent erysipelas Tenneson and Darier have observed lymph varices of the cheeks and mucous membrane of the mouth. They explain the condition as due to obliteration of lymph vessels or sclerosis of lymphatic glands.

Abscess of the superficial lymphatic glands is a common occurrence in erysipelas, and hardly needs detailed description.

DIAGNOSIS.—Difficult or usually impossible before the local lesion is developed, after that the diagnosis can almost always be made by inspection. When the general symptoms only are present, one should exclude as many other conditions as possible by the complete examination, and withhold the diagnosis or simply make one covering the most distinct local condition. As in all other cases, the examination of the pharynx should never be neglected, and when the general symptoms are present, with pharyngitis, the possibility of erysipelas should not be forgotten. Whenever there is a known wound or abrasion, still more, exposure to other cases, the symptoms of the onset should at once excite the suspicion of erysipelas. This is true also of coryza, in which chill, fever, vomiting, etc. occur without signs of other infectious disease. The examination of the lymphatics of the head and neck should not be neglected.

When the eruption has appeared, it is usually unmistakable, but there are enough anomalous cases to make a careful examination necessary always. The elevated redness, the increased consistence of the skin, the margin, which the patient often describes as spreading or which can be seen to spread from hour to hour, the fulness, itching, or tickling in the skin, the tenderness in the enlarged lymphatic glands in the vicinity, and the history of the onset, usually make matters clear. But sometimes some of these signs are absent or equivocal, and a differential diagnosis must be made. Usually a want of definiteness of the margin causes the greatest difficulty. This allows confusion between erysipelas and numerous forms of erythema and dermatitis, such as those from exposure to the sun, from irritating drugs, or from poisonous plants or animals. In most of these the redness is not so clearly outlined, the swelling if present is very superficial, the margin does not extend in so characteristic a manner. Finally, the general symptoms are absent. In the case of dermatitis from poisonous plants or animals a history can usually be obtained. The appearance in many of these cases is like that of erysipelas, but the swelling is not so deep.

Lymphangitis and erysipelas have a close relationship, and in erysipelas it is often possible to make out distinctly the existence of inflamed lymph vessels. In lymphangitis without erysipelas the absence of the characteristic elevation with progressing boundaries is important. Redness over a considerable area may be present, but is likely to be irregular in its outlines and uneven in intensity of tint, or even with areas of unaffected skin in it. In simple lymphangitis the temperature is not so high as in erysipelas, and the symptoms of the onset are usually not so distinct, though sometimes present.

It is difficult to distinguish between erysipelas and diffuse phlegmon of the skin. The latter may have an abrupt margin, but this is not so elevated and so distinct to the touch as in erysipelas. The redness is usually duskier than in erysipelas, and the swelling greater. The general symptoms come on more gradually, as a rule, but may be very severe.

Urticaria, mumps, and eczema, all of which have been mistaken for erysipelas, can be distinguished by careful attention to the local and general features of the different diseases.

The condition described by Rosenbach as *erysipeloid*, sometimes called migrating or chronic erysipelas, can hardly be mistaken for erysipelas if care be taken. This disease occurs especially on the wrists and hands of cooks, hucksters, fishermen, and others who handle irritating substances. It usually begins in the fingers as an infiltration with redness, and extends very slowly toward the wrists, often reaching them only at the end of a week or later. It subsides slowly without suppuration. Fever is absent.

Erysipelas of the mucous membranes can only be distinguished as such when its relation to erysipelas of the skin is evident. The distinction between erysipelas of the larynx and the so-called idiopathic œdema of the glottis is a matter of theoretical interest and does not affect the treatment.

PROGNOSIS.—The prognosis in erysipelas varies widely in different cases. The mild nature of most cases of facial erysipelas has made that disease a favorite among those who claim to work miracles in medicine. On the other hand, erysipelas is at times extremely fatal.

In making a prognosis one can be guided to a certain extent by the fact that a sporadic case is usually more favorable than one developing in an epidemic. The previous condition of the patient is of great importance. Even the most severe cases are recovered from by persons previously in good health. All temporary or long-standing conditions of debility, as convalescence from acute disease, drunkenness, atheroma, advanced malignant disease, etc., are unfavorable. Cases of chronic nephritis are usually extremely unfavorable subjects for erysipelas. Erysipelas in the first month of life is almost always fatal. After that time the danger decreases, but in old age it is again pronounced.

In any case it is unsafe to predict as to the probable time of recovery, and even when the temperature falls and the local process ceases relapses must be looked for. Erysipelas of the mucous membranes is more dangerous than that of the skin, and the danger is greater as the inflammation proceeds toward the deeper parts, as the larynx. Erysipelas of the scalp is in most cases dangerous simply because it occurs in severe cases. The occurrence of unequivocal symptoms on the part of the central nervous system must be looked for and used accordingly. Gangrenous and hemorrhagic erysipelas are unfavorable; suppuration, when tending to be circumscribed, is not so unfavorable. In both the gangrenous and phlegmonous forms even the most extensive destruction may be recovered from.

TREATMENT.—In the treatment of erysipelas two leading indications must be kept in view: the prevention of infection in others and the treatment of the patient. As regards the former, erysipelas is not so dangerous to others as most of the acute exanthemata, as predisposition is not so marked and infection at a distance is more rarely observed. At the same time, the erysipelas cocci have considerable power of resistance, and local or temporary predisposition is at any time possible. The infectious material is therefore to be destroyed as near as possible to its source, and the patient is to be treated to that end as any septic surgical case should be. In hospitals, erysipelas patients should be isolated, or at least separated from all others with wounds or diseases of the skin or mucous membranes. Dressings from such cases should be burned at once after removal; clothing and bedclothing should be disinfected. Instruments used on them should also be disinfected. Physicians and attendants should avoid getting secretions and discharges on their persons and clothing, disinfect their hands after examinations, and take special pains to avoid infection of wounds on their own persons. The existence of coryza or acute pharyngitis furnishes a source of danger during the care of an erysipelas case, and, although a certain amount of risk is unavoidable, much can be done by cultivating the habit of keeping the hands away from the mouth and nose. The greatest care must be taken by those who treat cases of erysipelas and obstetric or surgical cases, but if proper disinfection is practised, it is possible to treat all of these at the same time.

As regards the patient, the indications are to hasten the natural tendency to recovery, to relieve painful or dangerous symptoms, and to prevent or mitigate complications. Although one may entertain the hope that some more specific method of treating erysipelas will ultimately be discovered, our best methods at present are the outcome of clinical experience.

Marmorek[1] early in 1895 devised a method for obtaining an antitoxic streptococcus serum. This serum has been extensively used, especially in France, in erysipelas and scarlatina-diseases in which the prognosis is proverbially uncertain, so that the results must be accepted with caution. Many adverse results have been observed, and the experiments of Aronson[2] and Petruschky[3] are opposed to those of Marmorek, but indicate the need of further investigation.

Erysipelas is a favorite subject for therapeutic novelties, and an immense amount of ingenuity has been expended in devising methods of treatment, the very multiplicity of which shows how far they are from realizing the claims made for them, although the natural tendency to recovery gives favorable material for each method. The writer believes, however, that among the newer methods of treatment there is one at least of value, although not committing himself to all of the theories which have been announced in explanation of the results obtained. This method consists in the routine use of ichthyol on the skin, as proposed first by Unna, and since then used with satisfaction to a greater extent than any other contemporary method. The iron and quinine of tradition are no doubt useful, especially on account of the alcohol in the preparation of iron universally used, but in most cases alcohol is not necessary, and when it is can be given more rationally in a less complex mixture. That iron and quinine have any efficacy, as claimed by some, in promoting healing by phagocytosis, is altogether problematical.

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[1] *Annales d'Institut Pasteur*, 1895.

[2] *Berliner klin. Wochenschr.*, 1896, No. 32.

[3] *Centralblatt für Bakt.*, etc., 1896, Bd. xx. Nos. 4, 5.

The general care of the patient should be carried out on the lines followed in other acute diseases. The patient should be in bed, in a well aired room, not too warm. The room should be darkened if the eyes are affected. Cleanliness of the patient, his clothing, and his surroundings are essential.

The diet should be mild, but in quantities as large as the patient can digest, consisting largely of milk, with thin soups and gruels, albumen water, etc. If the patient is seen early enough, the symptoms of the onset must be treated. Vomiting should be encouraged by drinking tepid water until the stomach is empty, and then, if it continues be checked, by bismuth and lime water, carbonated water, bits of ice, or a mustard plaster over the epigastrium. It is usually advisable to give a mild calomel purge, followed by a saline, in the beginning of the disease.

After careful examination of the patient, and especially of the local disease and the treatment of wounds or ulcers on surgical principles, the ichthyol is applied. It is used most frequently in combination with vaseline, in the proportions of 20 to 30 per cent. This form is to be preferred in the majority of cases, but in delirious or unruly patients more adhesive preparations can be used with advantage. I have found the following formulæ useful:

Unna's Ichthyol Varnish.

℞. Ichthyol,	grm. 40.0;
Starch powder,	40.0;
Albumen (egg),	1.5;
Water to make	100.0.—M.

Or,

Ichthyol Traumaticin (Juhel-Rénoy).

℞. Ichthyol,	
Traumaticin,	equal parts.—M.

Before applying the ichthyol the skin must be cleaned with soap and water. The ichthyol is then rubbed or brushed over the skin at least three quarters of an inch from the red margin, and covering a strip about that width all around the lesion, then covering over the inflamed part.

The astringent action of the remedy is very soon evident. I have convinced myself it is much more marked than that of vaseline alone. In favorable cases the redness and swelling lessen, no extension takes place, and the general symptoms subside. If the margin advances, the ichthyol must be applied beyond it; usually it is not necessary to apply it more than twice a day. It should be kept applied until the temperature has been normal for two days, except in very mild cases, and always reapplied as soon as a fresh eruption occurs.

The application of the drug is sometimes painful, though not to be compared with that from nitrate of silver. Almost always the improvement in local and general conditions is so striking that the patient is ling to put up with the superficial pain and the unpleasant odor of he remedy.

It is probable that ichthyol owes its efficacy to its astringent and nterirritant properties, although according to Abel[1] it has a peculy marked action on erysipelas cocci. It is therefore comparable o nitrate of silver and iodine, to both of which it seems undoubtedly superior. Ichthyol also resembles in its action the constricting methods recommended in the treatment of erysipelas, but is much more convenent and simple than most of these.

In regard to its antiseptic properties, as used in erysipelas, ichthyol oes not prevent abscess of the skin and lymphatic glands. Abel advises that only freshly made preparations be used, as in the dilute form it does not remain free from bacteria.

In simple cases of erysipelas, even of the most severe kind, internal treatment is not necessary. The condition of the heart and urine must be carefully watched. If the pulse becomes weak or irregular or the heart sounds show indications of weakness, whiskey, strychnine, or small doses of quinine should be given.

In cases with prostration beef tea, eggnog, and other stimulants should be given as required.

Symptoms of nephritis must be treated as for an independent disease.

Old or cachectic persons and hard drinkers must be given stimulating food and medicine from the beginning.

For high temperature quinine in full doses or phenacetin can be used. Cold bathing or sponging is often beneficial.

For delirium the ice cap should be used, and if necessary bromide of potassium, with or without chloral to produce sleep.

Complications must always be looked for, especially when the case does not show signs of improvement within three or four days. When found, complications must be treated as independent diseases, the external ones, like abscess and gangrene, on surgical principles.

It is in the latter cases only that the more heroic methods of treatment are to be used. Such are injections of antiseptics or incisions with antiseptic compresses. In ordinary cases their use is uncalled for.

When erysipelas extends into the scalp, the hair should be cut short for convenience of applying remedies. As the hair will be lost in any event, there can be no objection to this. In other cases the hair need not be cut. Ichthyol used on the scalp should be diluted with water or oil.

For the nasal or pharyngeal complications of erysipelas antiseptic sprays and douches are to be used. Erysipelas of the larynx is treated by cold externally, ice pills, scarification, and, if necessary, tracheotomy.

After recovery from erysipelas the affected parts must be thoroughly cleaned. Abscesses or ulcers must be thoroughly treated, in order to remove all possibility of relapse by infection from such lesions.

Relapses should always lead to careful examination for some such source of infection. Next to these, the clothing or furniture may harbor the specific bacteria. Disinfection of the room should therefore be practised.

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[1] *Centralblatt für Bakteriologie und Parasitenkunde*, Bd. xiv., 1893, No. 13.

In convalescence remedies to increase appetite and digestion are often indicated. Frequently iron is useful in this stage.

The use of erysipelas cocci or their products in the treatment of malignant and infectious diseases belongs rather to the domain of experimental pathology and therapeutics than to practical medicine. From the results of Fehleisen, Coley, Emmerich, and others, who have experimented in the matter, it is clear that live cultures should not be used, since there is a chance, though small, of dangerous accident.

PYÆMIA.

By I. E. ATKINSON, M. D.

Definition.—Pyæmia (πῦον, pus, and αἷμα, blood) is a disorder dependent upon the presence in the blood and tissues of pyogenic organisms derived from a suppurative or infected centre in the body, and is characterized by inflammation of veins, thromboses, embolisms, and metastatic abscesses, accompanied by fever. It manifests itself by irregular chills, remitting or intermitting fever, sweating, and the development of secondary centres of inflammation and suppuration.

Etiology.—The connections between external suppurations and internal inflammations, and the ultimate effects of the poisoning of wounds, whether from putrefaction or otherwise, were recognized in very remote times. The crude ideas of pathology prevailing give no reasonable explanation of the causation of secondary inflammation and abscess formation. Toward the end of the last century John Hunter declared that pus gained admission to the blood through inflammation of veins, and ascribed the symptoms of what is now known as pyæmia to phlebitis. The theory that general purulent infection was dependent upon phlebitis gradually gained acceptance, and "pus in the blood" was held to be the pathogenetic factor. This theory led to the introduction of the term "pyæmia" by Piorry—a term that now serves to designate a special form of blood infection, though with a significance different from the original conception. Virchow, denying the presence of pus in the blood and agreeing with Cruveilhier that thrombosis was the initial lesion in pyæmic processes, made the first great advance toward a correct knowledge of their pathology. While erroneously asserting that coagulation of blood in veins preceded inflammation of their walls, he described the disintegration of thrombi thus formed, the detachment of parts of these and their escape into the venous circulation, the impaction of these particles in branches of the arterial system of too narrow calibre to transmit them, and the subsequent inflammation and suppuration of the tissues surrounding these embolisms. Today these are considered the essential pathological change of pyæmia; but the etiological basis of those changes remained unrecognized—indeed, could not be recognized—until the discovery of the influence of micro-organisms in pathogenesis enabled research to be prosecuted along the right line. Since the discovery by Klebs in 1870 that pyæmic processes are invariably associated with the presence of definite micro-organisms the dependence of these processes upon micro-organisms has been abundantly proven, and it is now known that they are those that excite supative inflammation. These micro-organisms of pus are of many ieties, but those almost constantly found are *staphylococcus pyogenes eus* and *streptococcus pyogenes*, the former most frequently the cause cumscribed abscess formation, the latter of rapidly spreading sup- on. As causes of pyæmia these two micro-organisms occur in about proportion, and one or the other will be found in nearly every case. e are, however, other micro-organisms which occasionally, though y, determine pyæmic manifestations; thus, the bacillus of typhoid "has been found in pure culture in osteomyelitis of the ribs, in purulent otitis media, in abscess of the soft parts, in the pus of ema, and in localized fibro-peritonitis either during its course or sequel of typhoid fever."[1] Likewise the *bacterium coli commune, nicrococcus lanceolatus, gonococcus*, and others are occasionally dis- d in suppurative processes in remote regions of the body. Prac- , however, pyæmia depends upon staphylococcus pyogenes aureus eptococcus pyogenes. Senn reports from the observations of Baser others 46 cases of pyæmia, in 22 of which staphylococcus was found, in 21 streptococcus; in 3 both organisms were present. Experi- ntal research has definitely shown that these bacteria are the actual ses of pyæmia. A pure culture of staphylococcus pyogenes aureus ected into a vein of a rabbit will be followed, pretty certainly, by ical and fatal pyæmia within three days. If, however, the culture, etimes indeed in considerable quantity, be injected into the sub- neous cellular tissue of animals, pyæmia is by no means certain to w, and if injected into the abdominal cavity of the dog, if care be n to avoid injury and the introduction of other foreign substances, e amounts of culture fail to produce any reaction. If, however, the culture be introduced into the abdominal cavity along with the bits of potato upon which they have grown, or if the intestines be injured so as to disturb the circulation, fatal peritonitis will ensue (Halsted). It often happens that pure cultures of pyogenic bacteria disappear after their introduction into the body without producing any noticeable reaction, but if they are introduced into the circulation along with minute particles of some indifferent substances, such as pith or cinnabar, or if the endothelium of the heart or of the bloodvessels is mechanically injured, typical pyæmia with metastatic abscess will ensue. The healthy tissues of animals have then the power to resist and destroy pathogenic organisms to a considerable degree. If introduced in small quantity into the blood, bacteria may be attacked and destroyed by the leucocytes of the healthy body.

It is probable that pus organisms gain admission to the circulation very commonly, in the presence of local suppuration, without injurious effects, and it has been shown that in septicæmia progressiva unlimited numbers may exist in the body without the development of pyæmia. So long as the epithelium of the bloodvessels remains intact conditions for pyæmia do not exist. It is true that when progressive septicæmia is unusually protracted bacteria become implanted in the vascular walls, and excite such changes in these by their toxic products that thrombotic phlebitis is set up and conditions for the development of pyæmia established; or the pus organisms may so modify the red blood corpuscles, in rabbits at least, as has been shown by Koch, as to bring about primary coagulation and the subsequent formation of embolic abscesses from the arrest of these coagula in small arterial trunks.

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[1] Abbott, *Principles of Bacteriology*, 2d ed., p. 231.

However it may occur, injury to the walls of the bloodvessels is essential to the production of pyæmia. As was first clearly shown by Virchow, the essential basis of pyæmia in man is thrombosis and the dissemination of the disintegrated thrombus in the circulation, where its fragments are carried along in the blood stream until they finally obstruct arteries too small to transmit them, and form embolisms which become centres for metastatic abscess formation. But simple thrombosis cannot result in pyæmia, and the embolisms caused by its detached fragments cannot determine metastatic abscess. Even the thrombosis and embolism caused by aseptic solid foreign substances, such as cinnabar, powdered charcoal, wax, etc., are incapable of inducing suppurative changes. Hemorrhagic infarctions and circumscribed necrosis may result, but nothing more. Pyogenic organisms must pervade the thrombi and emboli in order that pyæmia may develop.

Simple stasis of blood in a vessel is not sufficient to bring about coagulation. So long as the endothelium of the vessel remains intact and foreign bodies are excluded from its lumen this does not occur. Mechanical, chemical, or physical injuries to the vessel wall (particles of wire, needles, etc.), of pre-existing clots, parasitic organisms, changes in the blood or blood supply entailing disease of the vessel wall are the influences that bring about thrombosis. In pyæmia the influence that determines thrombosis is phlebitis. From a suppurative focus inflammation proceeds to involve the vein, advancing from without until the endothelia are reached; the toxins produced by the pyogenic microbes induce inflammation of its coats and coagulative necrosis of its endothelia. Upon the roughened endothelia a layer of hæmatoblasts forms the basis for coagulation. Upon this the leucocytes accumulate, fibrin is formed, and a white thrombus is established and projects into the lumen of the vessel, which is presently obliterated by the formation of a red thrombus. Coagulation now extends in both directions as far as, and often extending into, the nearest communicating veins. This thrombus is infected by pyogenic organisms, and inflammation extends along the vascular wall in contact with it. The thrombosis extends in a proximal direction until large veins become involved; it may even reach the *vena cava*. Usually, however, the proximal end of the thrombus projects into the lumen of a still patent vein, and is washed by its blood current. An infected thrombus has no tendency toward organization: it is loosely held by the venous wall, and is more or less disintegrated by the pus organisms and pus cells imbedded in it and surrounding it. Suppurative phlebitis may be restricted to the locality primarily affected, or the reproduction and growth of the micro-organisms may be inhibited by vigorous resistance on the part of the leucocytes and tissues, and further development may be prevented; but often particles of the original thrombus separate or are broken off by the blood current in the communicating vein, and with their contained micro-organisms are carried along with the blood toward the heart and arterial circulation. Sometimes only a few of such thrombotic particles are thus detached; at other times their number is very great. They may be very minute or so large as to be arrested in their passage through the heart.

In the constantly enlarging branches of the venous system no obstacle to their passage is offered. They pass through the right chambers of the heart, and are finally arrested in the arterial system at a point where the diminishing calibre of the branching arteries is no longer capable of transmitting them. Obviously, the first obstacle they meet is in the ramifications of the pulmonary artery. The size of the thrombotic fragments will determine the location of the plug or embolus in the pulmonary arterial system, and their number, the number of pluggings or embolisms. One may be so large as to obstruct the pulmonary artery at its earliest bifurcations. On the other hand, fragments may be small enough to pass through the pulmonary capillaries, enter the arterial current, and become arrested at some remote point in the arterial system. Arterial embolism, however, may also occur by the escape, through the pulmonary circulation, of pus organisms and leucocytes impregnated with pus organisms, which may become implanted in the vascular wall and excite thrombo-arteritis and suppurative inflammation.

When a portion of a thrombus plugs a branch of the pulmonary artery the circulation is at once arrested as far as the nearest communicating branch. If too small to obstruct the lumen of the vessel completely, obstruction is presently rendered complete by a secondary thrombosis excited by the embolism and blood stasis. Collateral circulation is not established in the lungs on account of the terminal character of the arteries of the pulmonary system. The thombosis, therefore, extends as far as the capillary distribution of the plugged artery, and a wedge-shaped area is established in which the circulation is brought to a stand. A scanty supply of blood wells into this area from the surrounding capillaries, and a hemorrhagic infarct is formed, with its apex at the point of the embolism and its base distal to it. It is at first pale, but soon becomes red from hemorrhagic infiltration. The pyogenic organisms entangled in the embolism—or, more correctly, their septic products—now excite a new set of changes. They are reproduced, and induce an inflammation of the arterial coats spreading from within outward—an infective arteritis.

The tissues surrounding the vessel are next invaded by suppurative inflammation, and an embolic or metastatic abscess is established, involving the infarct and spreading beyond it, leucocytes becoming pus corpuscles and the lung tissue necrotic. Such an abscess will ordinarily correspond to each embolism. If any portion of the secondary thrombosis project into a vein through which the blood still courses, fragments of it may become detached in turn, and carried to new localities, where they will be arrested and determine new metastatic abscesses. [illegible] ordinarily, the spleen, kidneys, and liver, but any part of the body may be involved. These abscesses may thus be widely disseminated. [illegible] in general there are many abscesses of small size; [illegible] few, but large. When [illegible] [illegible] [illegible] the resulting abscesses [illegible] large or small. The sub-[illegible] with the primary suppurative focus by implantation of pus organisms from the blood upon the intima of the vessels. Endophlebitis, thus established, causing coagulative necrosis of the endothelia, excites parietal thrombosis, which narrows the lumen of the vein, and may end by completely obstructing it. From the thrombus formed in this manner infected emboli may be detached. Pyæmia in certain cases of progressive septicæmia may sometimes be accounted for this way, as also the sequelar femoral phlebitis of typhoid fever and other conditions. The primary focus may be very obscure and readily escape detection, or it may consist in what is ordinarily considered a perfectly innocuous centre. The following case affords an example:

A man, forty-five years old, had a limited but very intractable eczema of the left leg. On January 16th pain in the left calf appeared and became so severe that he went to bed. Pressure was very painful, but nothing could be felt upon palpation. On January 17th he remained in bed with intense pain in the leg and thigh. There was a well marked phlebitis extending from the tibial side of the leg just above the limit of eruption and extending to the middle third of the thigh. The vein was hard and corded, and its course was marked by a line of redness along the skin. Considerable œdema of the leg and foot developed. Fever appeared without chill, but never exceeded 100.5° F. January 21st he was seized with a sharp respiratory pain in the left side, and a friction sound could be heard over the painful area. There was frequent dry cough. By January 25th a crepitant râle could be heard over the dorsal and lateral base. This was followed by prune-juice expectoration. On the 28th there was tubular breathing. The femoral vein was occluded and cord-like as high as Poupart's ligament, and the entire extremity greatly swollen. No new centres of inflammation developed and the patient slowly improved.

Pyæmia rarely arises through infection by way of the lymphatics, but that it may thus occur can be proven by the occasional presence of accumulation of pus in deeply seated glandular structures and in the thoracic duct in the bodies of those who have died of pyæmia. More commonly the lymphatic glands offer barriers of protection against pyæmia. Pyæmia, especially the more chronic forms, may exist when one cannot possibly recognize a primary suppurative focus. Those well known varieties of which ulcerative endocarditis and acute infective osteomyelitis are striking symptoms, may be cited as examples. In such cases the pyogenic micro-organisms will have gained admission to the blood by some unrecognized external or internal suppurative lesion, and, not finding conditions favoring their development elsewhere, ultimately settle upon places of enfeebled resistance in damaged cardiac valves or in the endothelium of veins of the osseous system (usually near an epiphyseal line), where they rapidly develop a phlebitis and osteomyelitis, and at times, though fortunately rarely, a septic intoxication that may have destroyed life before suppuration could have had time to occur. As has been noted already, pyogenic organisms may enter the circulation without producing morbid results. Conditions for their growth do not obtain, and they are destroyed, probably by leucocytes. At times they find a *locus minoris resistentiæ*, and excite suppurative inflammation in other localities than those just mentioned. Thus the pleural, pericardial, and peritoneal cavities and various joints are frequently invaded. In these localities infarcts cannot be demonstrated. The infection probably occurs through implantation of pus organisms or infected leucocytes in the capillaries of the parts. Often purulent inflammation of these parts is the only evidence of pyæmic infection. Some tissues are quite insusceptible of secondary pyæmic inflammation. Metastatic abscess of the brain, of the testicles, etc. is very rarely observed. Sometimes the so-called "spontaneous pyæmia" develops in persons who have received a slight injury or have been exposed to various depressing influences, as chilling or wetting. These influences suffice to lower the normal level of resistance and offer the opportunity to pyogenic organisms, already present in the circulation, to find a favorable nidus for their development. An inflamed joint, an osteomyelitis, or an endocarditis thus arising serves as the starting point of general pyæmic infection, with metastatic abscess and the usual train of symptoms.

From what has preceded it is evident that the distinction between infective septicæmia and pyæmia is purely arbitrary: the differences are of degree and not of kind. They both depend upon the presence of the same pyogenic micro-organisms in the circulation. Pyæmia is a septic infection plus thrombosis and metastatic abscess—a septico-pyæmia. The course of pyæmia, similarly to that of septic infection, varies with the virulence of the bacteria and the susceptibilities of the infected individual. The more acute the pyæmia, the more numerous will be the metastatic inflammations and suppurations. In chronic pyæmia the secondary inflammations are usually less numerous in proportion to its longer duration. Etiologically, then, infective septicæmia and pyæmia are identical.

PATHOLOGICAL ANATOMY.—It is not always easy to trace the route by which the pus organisms have gained the circulation. A primary suppurative focus will nearly always be found—a wound, an abscess, an osteomyelitis, a uterine phlebitis, an internal ulceration, a middle ear inflammation, or other lesion will exist. If an open wound, it will have lost its healthy characteristics, will present a dry, dull appearance, and be bathed in a thin or fetid pus. Generally the veins in relation with the infecting focus will be inflamed and filled with coagula. The inflamed vein, however, may be so minute as to escape naked-eye inspection. The coats of the thrombosed vein will be thickened, and will have a yellow or greenish yellow appearance. Small hemorrhagic spots will be present in great numbers, and microscopic examination will reveal a copious infiltration of all the coats with pus corpuscles and micro-organisms, *staphylococci* or *streptococci*. The thrombus will be softened, not firm, reddish brown or yellow, and puriform, and will consist of granular matter, disintegrating red and white blood corpuscles, pus cells, and micrococci, scattered and in colonies. Purulent transformation of the leucocytes will have rendered the thrombus much less adherent to the vascular wall than would be the case in benign thrombus. The disintegration of the clot accounts for the ease with which fragments may have been detached from it, and also for the smaller size of the emboli characteristic of pyæmia. At times the phlebitis will have developed into a periphlebitic abscess. The softened clot will extend, sometimes, for a considerable distance along the venous connections. In the portal circulation the original focus may have been an appendicitis, an intestinal ulceration, and in the newly born infant an umbilical vein inflammation.

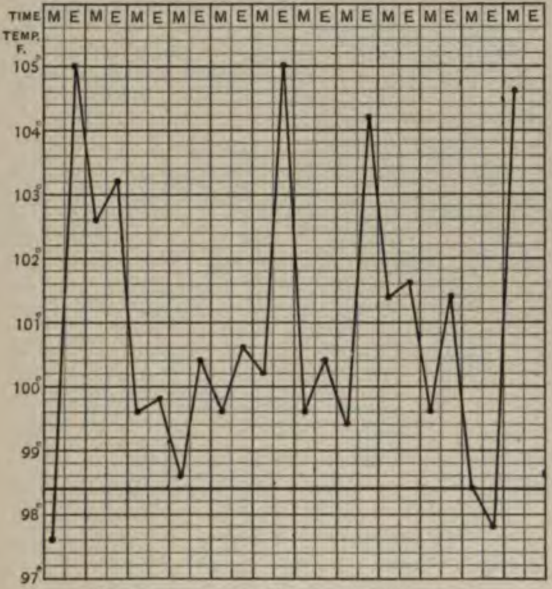
The embolisms will usually be found in the lungs at bifurcations of the pulmonary artery, and are generally centres of infarction. As they involve the smaller arteries for the most part, they are peripheral, wedge-shaped, and are not always sharply defined. Infarction is less apt to follow than in simple embolism. In multiple infective embolism infarction will be present at some centres, absent at others. Pulmonary metastatic abscesses are not often larger than a cherry, are usually situated in the pulmonary periphery, and involve the pleuræ, whence a purulent pleurisy may have originated. They are at first grayish in color, firm and surrounded by an intense hyperæmia; later, they form purulent foci. They become infiltrated with inflammatory products, the inflammation having extended from the intima of the obstructed artery until the whole area of the infarction has become implicated. The infiltration occurs by migration from the surrounding hyperæmic zone which bounds the abscess. This abscess contains a central necrotic mass and abounds in micrococci. The embolic abscesses of other parts are usually smaller than those of the lungs. They differ in shape and appearance. In the spleen they are small and often surrounded by a zone of inflamed tissue. They swarm with micrococci, and are of a dirty yellowish red color. Embolic abscesses of the liver, which, as involving ramifications of the hepatic artery, are most often a result of endocarditis ulcerosa, are small, yellow, wedge-shaped, and usually close to the capsule. Arising in the portal system, they are of larger size and few in number. The abscess is always separated from the surrounding hepatic structure by a zone of enlarged yellow lobules. Colonies of micrococci are present in the interlobular vessel and fill the capillaries for a long distance (Orth). Very few corpuscles are seen, the infarct being largely made up of liver cells. In the kidneys the abscesses are rarely larger than mustard seed, and are generally situated in the cortex, arranged in small groups, rarely in the pyramids—in the middle and outer portions. They are of a pale yellow color, and do not undergo softening, as their contents are not purulent, but rather masses of fatty degeneration. Micrococci will be found in them always.

In pyæmic arthritis the inflammation begins in the synovial membrane, and the pus is often ichorous. The membrane is swollen, reddened, and covered with pus. In the pleural, peritoneal, and pericardial cavities the inflammation speedily causes the accumulation of pus. Embolic abscesses of other structures may also be encountered, as in the skin, subcutaneous tissue, and the lymphatic glands, the parotid gland, etc. When metastatic abscess has occurred without embolism the suppurative inflammation will have originated in foci in the capillaries, where micrococci have invaded the epithelium damaged by the toxic substances in the blood, whence the inflammation has spread outwardly. Widespread coagulative necrosis will be found in pyæmia. The spleen is enlarged and softened, the heart flabby, and the mucosa of the intestines swollen and softened and the submucosa the site of numerous capillary hemorrhages. Purpuric spots will be observed upon the skin quite often, especially after ulcerative endocarditis. The brain and spinal cord and their membranes are rarely the seats of inflammatory changes. Suppurative meningitis, embolic abscess, and hemorrhagic effusions are rarely found. In ulcerative endocarditis of septic type micrococci pervade the vegetations on the valves or heart wall. When the right side of the heart is implicated, the small detached fragments may have caused embolism and metastatic abscess in the lungs; but from the left heart the embolisms involve the systemic circulation. Ulcerative endocarditis is often found without discoverable primary infective centre. As in infective osteomyelitis, the micro-organisms have found a habitat in the endothelia damaged and destroyed by coagulative necrosis. The secondary abscesses exist sometimes in great numbers; at other times only one or two may be found; again, ulcerative endocarditis may exist without embolism. The left heart is usually implicated in ulcerative endocarditis, though the right side is more often affected than in simple endocarditis. The endocardium as well as the valves may be affected. Vegetations, sometimes luxuriant, and ulcerations are the characteristic features. The vegetations are grayish yellow, very friable, and of varied conformation. They consist of fibrin and granular débris, cellular elements, blood cells, and micrococci. The ulcerations are irregular, may involve the myocardium, and even penetrate to the pericardium, or the cardiac septum may be perforated (Bramwell). Small abscesses are found at the bases of the vegetations in many cases. The organisms present are usually *streptococci* and *staphylococci*.

The intestines are not so frequently the seat of lesions in pyæmia as in septicæmia. Submucous metastatic abscesses are occasionally present, especially in the large intestine. These may open through the mucosa and form ulcers. Metastatic abscesses are often found in the muscular tissue, even in the walls of the heart, in the subcutaneous cellular tissue, the skin, and in the medullary cavities of bones.

SYMPTOMS.—Following delivery or a wound or surgical operation, pyæmia cannot develop until suppuration has taken place. This is commonly some time during the second week after external suppurative lesions, but after delivery during the latter part of the first week. Impending pyæmic infection is usually indicated by alteration in the appearance and behavior of the wound. The granulations will become pale, inactive, and unhealthy. The pus will lose its creamy character, and become thin and ichorous and scanty. The surrounding tissues will grow infiltrated and œdematous and somewhat livid. The lochia of the puerperal woman will become scanty and fetid or suppressed, the external genitalia hot and dry, and intrapelvic pain and tenderness develop. The patient will suffer from general discomfort and anorexia. There will be slight headache, elevation of temperature, and thirst. The tongue will have a thin, moist coating. The general symptoms will be ushered in by a chill more or less severe, and lasting from a few minutes to an hour or more. It may be limited to a chilly or "creepy" sensation. Thermometric observation will already show several degrees of elevation. In the great majority of cases the chill will occur in the daytime. The initial chill does not mark the occurrence of suppuration. It is probably due to septic absorption or to the circulatory changes consequent upon the entrance of infective material into the blood current. Later, the chills may indicate the formation of pus. The temperature may rapidly rise to 105° F. or more. More commonly it is not so high—102°, 103°, or 104° F. The maximum is often reached within a few hours. After some hours, usually not until the next day, the temperature falls nearly or quite to the normal, and a copious sweating follows. With or without chills the fever assumes an intermittent or remittent type, and is frequently confounded with malarial fever. The distinct periodicity of the malarial paroxysms is absent, however, and both chill and fever will vary in intensity; more than one chill may occur during the twenty-four hours (Fig. 41). After the first

FIG. 41.



Temperature record of pyæmia (Tillmanns).

day a chill may not mark the exacerbation. A very remarkable feature of the fever is its inequality: within a few hours the thermometer will mark changes of several degrees, though, as a rule, the morning temperature will be lower than that of the evening. The remissions are always marked by copious and persistent sweats; sweating, however, may be present almost continuously, and the bedclothes and bedding saturated with moisture. During the brief remission of symptoms the temperature may even fall one or two degrees below the normal. In more protracted cases a normal or subnormal temperature is sometimes maintained for a day or two, and excites illusive hopes of a permanent betterment, which, however, will be interrupted presently by a recurring chill with rapid elevation of temperature. Even in favorable cases permanent defervescence never occurs abruptly; it is reached gradually after repeated interruptions and exacerbations. The atypical character of the chills, the hot stage, and the sweatings place pyæmia in notable contrast with non-septic diseases.

The pulse will vary with the temperature. In mild cases there may be but little increase of frequency. It may not exceed 80 or 90, but will be soft and compressible. In severer cases it becomes very frequent, and, as the fatal issue approaches, more frequent, feeble, and compressible. An important feature of the pulse, and one characteristic of pyæmia, is that in the remissions of temperature a corresponding diminution in its frequency will not be observed. It will remain rapid even though the thermometer may indicate no febrile heat. In favorable cases the pulse returns to the normal very slowly. Microscopic examination of the blood will reveal, in addition to the presence of bacteria, some leucocytosis and increase of blood plaques, with diminution in the number of red blood corpuscles. The micro-organisms will be found in the plasma as well as in the white corpuscles.

During the earlier period the tongue remains moist and thinly coated. As the disease advances the coating becomes thicker and yellower, and when a milk diet has been pursued it may assume a dense cottony appearance. Still later the tongue may be dry and cracked, and when a typhoid state develops it may be brown, hard, dry, and cracked. Not unfrequently it is dry, red, and as if varnished. The teeth and gums may be covered with sordes, and the lips dry, fissured, and partly covered with brownish crusts. The breath has often a peculiar sweetish odor, which has been compared to that of hay. Nausea and vomiting are not always observed, but anorexia may remain complete, though liquid nourishment and medicines will be swallowed without complaint. Thirst is intense. Early diarrhœa is not so common a symptom as it is in septicæmia; later it is often established. Pus and blood in the stools indicate the existence of pyæmic intestinal lesions. Fetor of the stools sometimes is intense. The skin, which often glistens from the admixture of sweat and sebum, may be cold and clammy in the extremities. When sweating has been copious the flanks and abdomen are often covered with sudamina. The surface early acquires a dusky, sallow tint. This may be hepatogenous in part from catarrhal obstruction of the bile passages, but later it is principally due to disintegration of red blood corpuscles and liberation of pigment under the infective influence. Jaundice may become intense. Erythematous eruptions are sometimes observed. They are usually encountered in the vicinity of the primary suppurative focus, but may occur as a diffuse scarlatiniform rash, or may closely simulate erysipelas, constituting an infective dermatitis. Scattered papular and pustular (sometimes ecthymatous) eruptions often appear. Herpes facialis is a very common concomitant. In a more advanced stage a very distressing general hyperæsthesia may arise, so that the patient complains bitterly of movement or pressure. This hyperæsthesia is both cutaneous and deep, and does not depend entirely upon metastatic inflammation, which is often absent from the regions implicated. The urine is scanty, acid, high colored, and of high specific gravity. At the onset it is rarely albuminous, though albumin may be present as an expression of the febrile condition. Later it may become albuminous from involvement of the kidneys in metastatic inflammation. The splenic area is constantly enlarged; that of the liver much less frequently. Widespread joint inflammations often occur quite early in the disease, and not infrequently occasion such close simulation of articular rheumatism as to lead to erroneous diagnosis. Large and small joints may be attacked; probably those most frequently involved are the shoulder-joint and that of the knee and the sterno-clavicular articulation. The patient first complains of pain in the affected locality. More or less rapidly swelling will develop, and fluctuation may be detected. The circumscribed superficial redness of acute articular rheumatism will rarely be simulated. Upon incision of such a joint pus or sero-pus will be liberated.

The intelligence is rarely affected at first, and often remains unimpaired almost to the end. However, the patient is strangely indifferent to his peril, and may be surprised, annoyed, or, possibly, amused at the anxiety of his attendants.

In acute cases the disease runs its course within a few days to a fatal termination, and the patient may pass into a typhoid state and coma before local evidences of metastasis may have developed. But the duration of an attack is indefinite, and chronic pyæmia may last for weeks and months, to terminate in death, or, rarely, in recovery. Early thrombo-phlebitis may sometimes be detected in the vicinity of the infective focus through a painful, tender, hardened, cord-like vein. The occluded and inflamed larger veins may often be followed to the points where they disappear in the trunk, and can be marked out by the eye by the red line of cutaneous hyperæmia superimposed upon them. It is quite possible for the infective process to go no farther than this thrombo-phlebitis, and the patient finally recover, his blood and tissue cells successfully contending with and destroying the pus organisms and neutralizing their toxins by their own products. In such cases recovery will be slow and interrupted. The most important phlebitis of this character is phlegmasia alba dolens. It is most frequently observed after childbirth, but occurs under a number of conditions—after surgical operations upon the pelvic viscera, during the decline of typhoid fever, or after convalescence from this disorder has been established; in the course of tuberculosis, erysipelas, gonorrhœal rheumatism; after parenchymatous tonsillitis; during various infectious disorders; and, finally, as a result of purely septic infection. In all cases it is probably due to secondary infection by pyogenic bacteria. Except in cases of general septic infection and pyæmia its course is usually favorable. The symptoms of this phlebitis generally begin with pain, especially in the calf and in the groin. This is quickly followed by œdema of the limb, beginning in the foot and gradually ascending. In the great majority of cases the left lower limb is affected. The œdematous limb is pale and shining, and sometimes shows the blue tracings of veins that have been dilated in the establishment of collateral circulation. If the phlebitis has been primary, the detachment of a portion of its infected thrombus may serve as the starting point of pyæmia. These phlegmasiæ often subside quickly, but quite frequently, and especially after typhoid fever, œdema is very persistent and may lead to permanent enlargement of the limb with varicosity of the veins.

The occurrence of embolism will not be marked by symptoms, unless, as is very rarely the case, the attached fragment of thrombus is so large as to plug a large branch of the pulmonary artery; in which case, sudden dyspnœa, and possibly death, may occur. While embolism by an infected thrombus usually proceeds to suppurative inflammation, this will not be of necessity. Occasionally a thrombo-phlebitis will be followed by indubitable evidence of metastatic deposit in the lung, with pneumonic inflammation and even pleuritis, without the process advancing to suppuration. A limited area of pulmonary consolidation, marked by characteristic signs and even pleuritic friction sounds, with resulting effusion, will slowly undergo resolution and the patient recover perfectly. This will not happen, however, when the metastases are multiple.

The occurrence of metastatic abscess is marked by an aggravation of the symptoms and by recurrent chills and sweating. If the infarcts are small and scattered throughout the pulmonary area, their usual locality, their presence may not be revealed by physical signs. They may be inferred by an increase in the respiratory rate and by the appearance of the sputa. At first the sputum may resemble currant jelly, a result of hemorrhagic infarction. Later it may become offensive and purulent, and contain particles of lung tissue and elastic fibres. Only when the abscesses are large or when several coalesce can they be detected by physical examination. Cough will attract attention to the chest, and pain in the side will indicate the presence of pleurisy. The number of these abscesses may be enormous. Empyema may occur, and perforation of the visceral pleura may cause pneumo-pyothorax. Metastatic abscess of parts supplied by the systemic arterial circulation will be revealed rarely by physical signs. Intense pain in the splenic region may indicate the presence of splenic abscess, and the appearance of albuminuria may, but does not necessarily, announce the involvement of the kidneys in similar changes. On the other hand, renal embolic abscess may exist without albuminuria. Embolic abscess of the liver will hardly be detected, but may be inferred from slight enlargement and tenderness of that organ. If the infective focus involve the portal circulation, the abscesses that affect the liver, with or without pylephlebitis, may be large and protracted in their course, causing jaundice, hepatic enlargement, sometimes palpable fluctuating tumors, and a typhoid state. Embolism of the intestinal canal will rarely present symptoms excepting diarrhœa. If a large artery have been obstructed, there may occur nausea, vomiting, pain, and tympanites (Osler). Embolic abscess of the brain is rare in pyæmia, though more common when it is associated with ulcerative endocarditis. The symptoms are obscure and depend upon localization. In the general disorder they are apt to escape observation unless accompanied by paralysis. In some cases of pyæmia, especially that occurring as a complication or sequel of typhoid fever, suppurative inflammation of the parotid gland occurs. In the most acute cases death often anticipates the formation of pus in this gland.

The presence of metastatic abscess is inferred from the persistence of symptoms, the recurring chills with varying temperature, and the exhausting sweating, when it is not manifested by local signs. In its further course pyæmia is characterized by a continuation and, if acute, by rapid intensification, of all the symptoms. The range of temperature will be great, varying sometimes from five to six degrees during the day, rising and falling several times, sometimes with intermissions, during which the temperature may be subnormal, with free sweating and perhaps symptoms of collapse. In the more acute cases, while chills may occur several times during the twenty-four hours, the temperature rarely reaches the normal, but in the exacerbations it may attain 104°, 105° F., or more. The pulse varies with the temperature, becoming gradually more frequent and feeble as the fatal issue approaches. In acute cases death generally occurs within a week or ten days. When metastatic abscesses are few the course of the disease may be very protracted. In such cases the symptoms are uniformly milder; the daily range of temperature is not so great. Very often a distinct intermission will be observed, during which the temperature may remain normal or subnormal for hours at a time. Chills may or may not recur daily, and in the remission of fever the copiousness of the sweats may be less.

In puerperal pyæmia, in which infective phlebitis usually begins in the veins at the placental site by bacterial invasion of the thrombi, the disorder may develop very insidiously from a slight endo- or parametritis, usually during the first week of childbed. The symptoms begin with a chill, which may be protracted and severe. Apart from the symptoms of intrapelvic inflammation, the course of the established disease is that of ordinary pyæmia. Peritonitis is generally absent. Death usually occurs during the second or third week, but recovery may follow after more or less prolonged illness in cases where metastasis has been slight and has not involved the more important organs (Lusk).

Many of the milder forms of pyæmia, such as occur in typhoid fever, scarlet fever, etc., pursue very protracted courses. The occurrence of chills after the third week of typhoid fever more often than not signalizes the engrafting of septicæmia or pyæmic processes upon the original disease; and, although pure cultures of the typhoid bacillus have been obtained from suppurative foci in this disease (evidence that this bacillus is also a pus organism), commonly typhoid and post-typhoid parotiditis, femoral phlebitis, pylephlebitis, etc. are of distinctly pyæmic origin. Similarly, the suppurative joint inflammations, etc. after scarlet fever are evidences of secondary pyæmic infection. The milder pyæmic infections that arise in this manner usually pursue a favorable course, but, as a rule, even in chronic pyæmia the course is unfavorable. The patient finally becomes exhausted by the toxicity of the disease and the fever. He grows profoundly prostrated, emaciated, and anæmic; bedsores, furuncles, and subcutaneous abscesses may develop before death.

Osteomyelitis, which is generally an affection of childhood, or, occurring later in life, a recurrence from childhood and due to encapsulation of pyogenic organisms after the original attack, or, as is more probable, a reinfection in a *locus minoris resistentiæ* from the blood current, may exhibit only pain and the symptoms of acute septic infection and a rapidly fatal course. But it may also constitute one of the phenomena of ordinary pyæmia, and, on the other hand, rarely it may serve as the centre for general pyæmic infection. Cases in which infection of several centres of the osseous system by pyogenic bacteria occurs are not so very uncommon. They are not, strictly speaking, truly pyæmic, and follow a much more favorable course.

The more protracted cases of pyæmia are often very obscure. It is here that errors in diagnosis are most often made, especially when the primary focus has escaped observation. Chronic forms of pyæmia may originate in pyelo-nephritis, intestinal ulcerations, and various suppurative centres in internal parts of the body, and present symptoms closely resembling those of typhoid fever, tuberculosis, etc.

The most interesting form of chronic pyæmia, however, is malignant or ulcerative endocarditis. This may occur as a frank secondary symptom of pyæmia, or it may be the primary lesion and infective focus. Though it may proceed to a fatal termination within a few days as part of an already disseminated pyæmia, or even as a primary affection, its course is often prolonged for many weeks and even months. When secondary, following a wound, a surgical operation, or suppurative puerperal lesion, no modification of the ordinary course of pyæmia may be observed. Should the life of the patient be prolonged, however, embolisms from the endocardial surface, sometimes in countless numbers, may be swept into the circulation, and small metastatic abscesses evoked in the various organs and parts of the body.

Its presence will usually, but not always, be recognized by the development of an endocardial murmur. In the great majority of cases the left side of the heart is implicated. In 209 cases referred to by Osler in his Gulstonian Lectures, the left valves were affected in 171 cases, the right valves in 34. In 9 cases the right heart alone was involved. Pyæmic endocarditis usually arises in hearts that have already been damaged and afford a favorable nidus for the growth of pus organisms. It rarely begins as a primary endocarditis. The symptoms are often extremely vague and misleading. They may begin abruptly or insidiously, with chills, pyrexia, sweats, all of irregular and atypical character, and pass gradually into a typhoid state. As a rule, subjective cardiac symptoms are slight; they may be altogether absent. Palpitation, præcordial distress, and pain are occasionally present (Bramwell). Sometimes the symptoms are pronounced, and at once direct attention to the heart. The earlier general symptoms have often a close resemblance to those of malarial fever; all phases may be closely simulated. In the absence of embolic symptoms they may be readily mistaken for typhoid fever. During the course of the affection great variability of the cardiac murmur will often be observed, and affords a significant aid to diagnosis. These cases may be protracted for months. They may not exhibit symptoms of metastasis until near the end. More acute cases rarely run their course without metastasis. The absence of a heart murmur throughout is not so very uncommon. Then an early diagnosis is quite impossible. Later, ulcerative endocarditis may be inferred by exclusion or determined by evidences of arterial metastatic inflammation. Ulcerative endocarditis may endure days, weeks, or months, gradually exhausting the patient with recurring rigors, pyrexia, and sweats, until he passes into a state of profound prostration, coma, and death.

The temperature by rapid changes may pass from the normal to 105°, 106°, 107° F., or more. A continuous high temperature is sometimes maintained. Nearly always, sooner or later, the symptoms will be modified by those of metastatic inflammations. Excepting when the right heart is involved these will develop in the systemic arterial circulation, justifying the term *arterial* pyæmia suggested by Wilks. The lungs are, naturally, much less frequently the seat of infarcts than in ordinary pyæmia, but pneumonia, pleurisy, and empyema are not uncommon concomitants. Delirium, paralysis, coma will indicate cerebral and meningeal metastasis. Local and general symptoms will for the most part be those of general pyæmia. Multiple cutaneous and subcutaneous abscesses, and often, toward the end, innumerable cutaneous hemorrhages forming purpuric spots, will not infrequently develop before death. Sometimes gangrene of the extremities will indicate the occlusion of large arteries by emboli from the valvular vegetations. Parotiditis sometimes forms a symptom.

With the establishment of some or all of these symptoms the condition of the patient becomes more grave. Chills, varying pyrexia, drenching sweats, diarrhœa, hebetude, delirium, coma, succeed until the patient finally succumbs, usually within four or five weeks. Practically, recovery never follows. All cases of ulcerative endocarditis in which pus organisms pervade the endocardial vegetations, and ulcerations and their resulting embolic infarcts, may fairly be considered pyæmic, whether originating with rheumatism, old endocardial disease, or otherwise.

DIAGNOSIS.—Pyæmia is very often mistaken for other affections; most commonly for septicæmia, intermittent and remittent malarial fever, typhoid fever, acute miliary tuberculosis, and acute rheumatism. The diagnosis from septicæmia may at first be impossible. Indeed, progressive septicæmia may pass into pyæmia by the development of thrombosis and embolism, and, conversely, more or less septic intoxication and infection is present during the progress of pyæmia. Septic intoxication generally develops within a few days after a wound or injury and after the beginning of gangrene, and is dependent upon putrefactive as well as suppurative foci. Pyæmia is due to suppuration, and usually does not occur earlier than the second week of the wound or injury or suppurative lesion. The course of septic intoxication is briefer, and is without local manifestations. In progressive septicæmia chills are not nearly so often observed as in pyæmia. Pyæmia runs a more protracted course, but differentiates itself by the establishment of thrombosis and embolism and metastatic abscesses. The fever of septic infection is more continuous and attains a higher degree within a few hours. Its duration is much briefer, and when it is prolonged a pyæmic condition is often established.

Microscopic examination of the blood affords a ready method of distinguishing malarial fever from pyæmia. The presence of the plasmodium malariæ will establish the diagnosis. The distinctly intermittent and remittent character of the fever of pyæmia is the cause of many mistakes. In the more acute forms of pyæmia doubt will be dispelled by the course and development of the essential symptoms of the disease. The diagnosis from symptoms alone is often very difficult in the more chronic forms; but, apart from the microscopic diagnosis, the irregular development of chills, fever, and sweating, even without the secondary local manifestations, will not long justify hesitation between the two affections. Moreover, as Osler has well said, if a supposed case of malarial fever persists despite the full exhibition of quinine after several days, other causes than malaria must be sought for. Chronic cases may readily be mistaken for typhoid fever. Resemblance may be heightened by abdominal symptoms—diarrhœa, tenderness in the right iliac fossa, splenic enlargement—delirium and the typhoid state that is so often observed, especially in malignant endocarditis. It is very important to remember that frequently after the third week of typhoid fever a true pyæmia or septicæmia may be engrafted upon the original disorder. The occurrence of chills and the intensification of symptoms during the latter period of typhoid fever is very often due to septic or pyæmic absorption from the intestinal ulcerations. Post-typhoid parotiditis, phlebitis, etc. are usually pyæmic. Except in protracted cases of pyæmia the course of the fever will soon remove uncertainty from the diagnosis. In acute tuberculosis pyæmia is sometimes suspected at first. The course of the former affection, while occasionally very rapid, is always more regular than that of pyæmia. The expectoration, and often the discharges when present, will reveal the bacillus of tuberculosis. Acute rheumatism may be confounded with pyæmic arthritic inflammation. Post-scarlatinal and gonorrhœal purulent arthritis are usually pyæmic, the latter inflammation sometimes due to metastasis of the *gonococcus*.

When the primary suppurative focus has been apparent pyæmia is usually recognized without difficulty, but when this centre has escaped observation or has been beyond its reach, much obscurity often exists. Originating in osteomyelitis, pyelitis, pylehepatitis, or in any of the so called spontaneous manners, the keenest powers of observation will be necessary. In malignant endocarditis the diagnosis from typhoid fever may, for a time, be impossible. The purpuric eruptions of the endocarditic pyæmia have caused this disorder to be mistaken for typhus fever, cerebro-spinal meningitis, or malignant specific exanthematic fever. Hepatic intermittent fever—which, indeed, is probably a mild septic or at least fermentation fever—the fever of rapidly developing cancer, Hodgkin's disease, and the fever of local suppurations of whatever nature may at times simulate pyæmia.

PROGNOSIS.—The prognosis of pyæmia is unfavorable. Death will usually occur before the end of the second week, sometimes during the first. In chronic pyæmia the prognosis is less absolutely bad, though most cases end in death, sometimes after weeks and even months. The course of malignant endocarditis and of pyæmic cerebral suppuration is uniformly fatal; of the former rarely later than three or four months, usually within as many weeks. Where the primary suppuration focus is within the reach of surgical treatment, and the metastatic abscesses are few in number and not situated in vital parts, recovery may take place, though slowly. It cannot be denied that a thrombo-phlebitis following a primary suppuration in its turn may be followed by symptoms of embolism in the lungs and elsewhere, limited, however, to one or two foci, and yet recovery eventually take place. In such cases it can only be presumed that the micro-organisms of the thrombus and of the embolus have been of feeble virulence, and have been destroyed by the bactericidal action of the blood and leucocytes. The prognosis is much more favorable when metastatic abscess affects a part within reach of the surgeon's knife, as in metastatic parotiditis.

TREATMENT.—*Prophylaxis.*—The basis of modern surgery is in the avoidance of influences that permit the infection of wounds and the admission to the circulation of septic and pyogenic organisms and their toxic products. The most certain guarantee of protection to the individual is the maintenance of a rigid asepsis in uninfected lesions and the antiseptic treatment of these when conditions of sepsis or suppuration prevail. The prevention of suppuration in a wound furnishes absolute protection against pyæmia (Senn). The details of necessary treatment to this end are strictly surgical, and need not be considered here. Aseptic and antiseptic treatment in internal medicine has a much more restricted field, and is limited to a more or less ineffectual disinfection of the alimentary canal. Some measure of success may be expected in septic and suppurative lesions of the mouth, nares, and fauces, as in diphtheritic and scarlatinal inflammations, but it is doubtful if antiseptics can be administered in sufficient and safe quantities to effectually disinfect the intestinal canal. To the mouth, throat, and nares applications of hydrogen dioxide, corrosive sublimate, carbolic acid, sulphurous acid, and other bactericidal agents are universally employed, but no substance should ever be applied to these parts in such strength as to exercise a caustic action or in such a manner as to disturb mechanically the relation of the parts, lest absorbing surfaces be laid bare and the entry of micro-organisms and their products to the circulation facilitated. Numerous plans for preventing general infection through ulcerating surfaces in the intestinal canal, as from dysentery, typhoid fever, etc., have been proposed. It has been asserted that effective antiseptic treatment of this canal may be secured through salol, naphthalin, beta-naphthol, calomel, and other drugs. That some such influence may be brought to bear may be inferred from the positive deodorization of the stools that may be secured by these means, but there is little evidence of satisfactory antiseptic results. Salol in doses of from 60 to 80 grains daily, naphthalin in daily doses of from 1 to 2 drachms, beta-naphthol in 40-grain doses daily, have all been extolled for this purpose. Lately calomel has been recommended as an intestinal antiseptic, possibly through its conversion into corrosive sublimate. It can hardly be hoped, however, that an efficient antiseptic effect can be afforded by such measures.

The Treatment of Pyæmia.—The first objective point is the treatment of the primary suppurative focus and the destruction of its power for further evil. Pus should be set free, tension relieved, and drainage secured, if practicable, and thorough disinfection established. Early operative interference is indicated in acute osteomyelitis. Disinfection of the uterine cavity should be attempted in puerperal pyæmia. Excision of thrombotic veins has been recommended by Klebs. To prevent detachment of infected thrombi absolute rest and the avoidance of disturbing manipulation should be insisted upon. Purely antipyretic drugs should never be given. The questionable advantage of the reduction of temperature is more than counterbalanced by the decided depression following their use. Agents that maintain the vital power should be administered. Quinine and iron seem to serve this purpose best. At the outset quinine should be given in full doses, 30 to 40 grains during the day, in divided doses. This dose may be repeated for one or two days, but after this not much advantage is to be obtained from such amounts, and the daily dose may

reduced to 10 or 12 grains. Large doses of iron seem to be very
iceable occasionally. From 15 to 30 minims of the tincture of the
ide, well diluted with water, may be given every fourth hour.
preparation of iron seems to possess advantages over the others.
lic acid, salol, sodium benzoate, and many other remedies have
n urged, but their value is doubtful. Alcoholic stimulants will be
icated nearly always, and when the heart begins to fail strychnine is
ndoubted value. As there is no specific treatment of pyæmia, the
st important indication is the support of the powers of life by sys-
atic nourishment and stimulation. This holds especially in chronic
emia. The food should be the most assimilable possible. As the
n reliance nothing is so good as milk. From three pints to a half-
n during the day will be sufficient. Strong beef extracts, pepto-
ns, and peptonized foods will prove useful adjuvants, thus supporting
e patient until the infection has become exhausted. Whenever
condary infective inflammations are accessible they should be actively
eated surgically. Unfortunately, in the cases usually coming under
he care of the medical practitioner the infective centres are beyond
reach in the internal parts of the body. The successful treatment of
pyæmia is almost exclusively surgical. In the rare cases of recovery
the result is usually due to the feebleness of the infection, and the merit
of the physician depends upon his ability to supply to the sufferer support
in the form of nourishment and stimulation that will strengthen him in
is struggle against the morbific influences.

SEPTICÆMIA.

BY I. E. ATKINSON, M. D.

DEFINITION.—Septicæmia (σηπτικός, putrid, and αἷμα, blood) is an acute febrile affection depending upon the presence in the blood and tissues of organic chemical substances, resembling alkaloids, which are formed by minute organisms or bacteria which are also the causes of suppuration or putrefaction. These micro-organisms develop in foci in or upon the body, and excite in them suppurative or putrefactive processes and form poisonous chemical products. From causes that are not well understood these poisonous chemical substances, alone or along with the micro-organisms that produce them, gain admission to the circulation through lymphatics and bloodvessels, and produce morbid effects which are known as *septic intoxication*. Often this septic intoxication is intensified and perpetuated by the continued activity and reproduction of the accompanying micro-organisms within the body, whereby the supply of poisonous chemical products absorbed from the original focus is supplemented. The condition induced in this manner is known as *septic infection* or *progressive septic infection*. In pure septic intoxication no lesions beyond the original sources of contamination are produced; but in progressive septic infection minute areas of inflammation and coagulation necrosis in the vascular system will be excited; but the disorder is characterized by the absence of gross suppurative or necrotic lesions. When, however, death does not speedily terminate the infective processes, secondary centres of suppuration and necrosis sometimes develop. Septicæmia is then said to have become complicated with pyæmia, and the result has been called *septico-pyæmia*. With these processes must be considered one in which symptoms are produced indistinguishable from those of ordinary septicæmia, though milder and more transitory, which seem to depend upon toxic products of fermentations, possibly not bacterial in origin—the *fermentative fever* of Bergmann. Symptomatically, no sharp line of demarkation separates the mildest forms of surgical or traumatic fever or the irritative fever following absorption of poisonous products of putrid food substances and the most pronounced forms of septicæmia.

The stress of septicæmia is thrown chiefly upon the vascular and nervous systems and the blood, but the range of its activity is by no means understood, and probably includes most parts of the body.

ETIOLOGY.—Although the secondary results of wounds and injuries and suppurative and putrefactive processes generally upon the system at large have attracted the attention of writers ever since Hippocrates, and in many instances have excited shrewd guesses as to their parasitic origin, a scientific basis for their elucidation did not exist until Van

Leeuwenhoek in 1675 by means of a simple microscope discovered and described minute organisms which we now know to have been bacteria. The wide diffusion of such organisms at once, and naturally, suggested the dependence of many morbid conditions upon them. Such conceptions, however, were based solely upon speculation, and presently fell into disfavor, and were soon almost forgotten. Active interest in minute organisms as possible causative influences of disease was not again awakened until the present century had well advanced. Meanwhile, however, much work had been done in the study of putrefactive and suppurative processes and their relation to secondary inflammatory and degenerative changes, but the results were of pathological and not of pathogenic interest. Among the eminent men engaged in this research may be mentioned John Hunter, Abernethy, Cruveilhier, Magendie, Haller, and Virchow. With the second half of the century renewed and scientific interest in minute organisms as pathogenic influences received a stimulus from Davaine's discovery in 1850 of the anthrax bacillus in the bodies of animals affected with splenic fever, and the investigations in 1857 of Pasteur demonstrating the agency of bacteria in fermentative processes. In 1866, Rindfleisch described the presence of micro-organisms in local inflammatory deposits in the body. Von Recklinghausen, Waldeyer, Birch-Hirschfeld, Hueter, and others followed immediately with important observations revealing the presence of bacteria in pyæmic conditions. In 1870, Klebs described as *microsporon septicum* the bacterium which he had detected in the blood and tissues after wound infection, and differentiated septicæmia and pyæmia. The pathogenic influence of bacteria was now universally recognized, and Koch's observations in 1870 established a scientific basis for bacteriology in relation to pathological processes.

Koch's experiments with septicæmia of mice showed that the animal surely died in from eight to sixty hours (depending upon the virulence of the injected fluid) after subcutaneous inoculation with putrefying fluids. The result depended upon the stage of putrefaction. Blood that had been putrefying five hours in five-drop doses killed in eight hours without producing macroscopic pathological changes and without the development of bacteria in the blood or tissues; while blood taken from the auricle had no effect if introduced under the skin of another healthy mouse. Smaller doses, one to two drops, of the putrid fluid caused death in from forty to sixty hours. He found that by injecting the blood of the mouse thus destroyed he could propagate the virus indefinitely and in undiminished virulence, even in doses as small as one tenth of a drop. Different varieties of bacteria were found in the blood of mice made ill by the injection, but when death resulted small bacilli alone could be found. Gross lesions were never found, but in capillary bloodvessels alterations were produced resulting in extensive blood extravasations (Senn's *Principles of Surgery*). Koch also succeeded in causing septicæmia in rabbits by injecting into their tissues putrid infusion of meat, whereby changes similar to those induced in septicæmia of mice were brought about. The organism found was an oval micrococcus which invaded, and sometimes completely obstructed, capillary vessels. Cultures of this coccus introduced into another rabbit evoked similar symptoms.

A variety of other micro-organisms have been proven capable of causing septicæmia in animals; for example, *micrococcus lanceolatus*, originally described by Sternberg, and often present in the mouths of healthy persons, but also found in croupous pneumonia, cerebro-spinal meningitis, otitis media, and other diseases, and *micrococcus tetragenus* of Gaffky from healthy saliva and the sputa of tuberculous patients.

Pasteur in 1880 first cultivated *streptococcus* from the organs of women dead of puerperal fever, and it is now well established that in the great majority of cases of human septicæmia this pyogenic micro-organism is the pathogenic factor. But it is also certain that a number of other pyogenic bacteria may determine the same results. First among these is *staphylococcus pyogenes aureus*. These two bacteria will be found to be the causes of nearly all cases of septicæmia. Occasional causes of septicæmia are *staphylococcus pyogenes albus*, *gonococcus*, *micrococcus lanceolatus*, *bacillus pyocyaneus*, and others. But almost at once it became apparent that the fatal character of the infections could not depend upon the mere presence of these organisms in the blood and tissues, for they could be detected usually in only limited numbers, and often enough very careful research failed to reveal them at all, except at original foci or after death, in animals that had unquestionably been affected with septicæmia. It became evident, then, that if the bacteria themselves failed to account for the results, the explanation had to be sought in some poisonous substance concurrent with them, and probably produced by them. The conception of the action of poisonous chemical substances elaborated by bacteria upon the animal body received its impetus from the discoveries of Pasteur regarding putrefaction and fermentation. Research has shown that characteristic symptoms of sepsis may be evoked in animals by the injection of putrid fluid from which living organisms have been carefully excluded by sterilization, as well as of sterilized cultures of pyogenic organisms. Indeed, definite chemical substances which have been called ptomaïnes, toxic alkaloids, toxins, have been obtained from the putrid liquids, and have been proven to be capable of exerting poisonous influences over animals subjected to their action. Brieger and others have isolated a number of such products. Clinical observation appeared to justify the conclusion that similar toxic effects are frequently produced in man, and that a distinct form of septicæmia exists which is an intoxication produced by the absorption of the chemical products of putrefaction and suppuration, and in which no infective invasion of the blood itself by putrefactive and pyogenic organisms occurs. Such septic intoxication is widely held to depend upon putrefactive processes alone, in which bacteria are not to be found in the blood, or, if so, are only accidentally present and are innocuous. They are saprophytic bacteria, and can only grow in necrotic and putrefying foci exposed to the air. The intoxication, being caused by toxins (ptomaïnes) formed in these foci and absorbed into the blood, results in death or recovery just as the dose has been great or small. If this be small and the supply restricted by the removal or destruction of the putrefactive centres, recovery will probably follow; but if it be large and the supply continuous, the patient will probably die. This form of septicæmia is more especially encountered in puerperal fever, where the toxic material has been derived from putrective changes in the cavity of the uterus following delivery. Its supsed origin in saprophytic bacteria suggested to Matthews Duncan the me *sapræmia* (σαπρός, putrid, *αἷμα*, blood), by which it is widely own. There is some reason to believe, however, that septic intoxication is not so constantly dependent upon the organism of putrefaction as this term would indicate, as in typical "sapræmia" Bumm, Von Franque, and others rarely failed to find in the toxic centres pyogenic bacteria.[1] It is also significant that *proteus vulgaris*, a widely distributed micro-organism of putrefaction, according to Flexner, "may be unassociated with other bacteria in abscesses and in peritonitis, and it may cause general infection by invading the blood and internal organs."[2] When pyogenic bacteria are the cause of septic intoxication, it is by no means certain that the circulation remains free from them, but for some unexplained reason they are incapable of growth and reproduction in the blood; the suppurative centres furnish the toxins upon which the symptoms depend.

Not only may a septic intoxication depend upon absorption of the toxic chemical products of pathogenic bacteria, but it is known that similar effects, though in much milder degree, may be caused by ferment substances not bacterial in origin. Thus a febrile reaction may be excited by introducing into the blood of a living animal pepsin, trypsin, pancreatin, or a number of indifferent substances. The transitory fever that often follows within a few hours a wound, an injury, a surgical operation, even when there may be no external lesion, but especially after more or less extravasation of blood, the stomach ingestion of various injurious food substances, as so often occurs in children,—all may be supposed to be due to the absorption of various aseptic substances which Worm-Muller believes to cause by their action upon the blood the generation of fibrin ferment, which excites febrile reaction. This fever Bergmann denominates "*fermentation fever;*" Volkmann, *aseptic fever;* it is also known as *irritative fever*, *resorption fever*, etc. While it is quite possible, however, that this "fermentation fever" may be due to the absorption of "products of aseptic tissue necrosis," it is by no means certain that it may not ultimately come to be proven to depend upon a true septic intoxication of feeble potency.

Septicæmia in by far the greater number of cases is a *septic infection.* By this is understood a condition in which pyogenic bacteria gain admission to the blood and tissues, and there pursue their pathogenic activity. The common source of septic infection (progressive septic infection) is *streptococcus pyogenes*. *Staphylococcus pyogenes aureus* is also a frequent cause, but indeed any of the pyogenic bacteria may determine septicæmia. The best type of the disorder in the lower animals is anthrax, due to *bacillus anthracis*, in which the blood and tissues frequently swarm with the micro-organism. In septic infection the symptoms are due to toxins produced both at the original source of infection in the body and by the micro-organisms in the blood and tissues. The essential difference between a pure septic intoxication and septic infection consists in this, that the one cannot be inoculated upon another individual, while the other is freely inoculable.

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[1] Williams, *American Journ. Med. Sciences*, vol. cvi., 1893, p. 47.

[2] Welch, *A System of Surgery*, Dennis, vol. i. p. 322.

In man, in septic infection the number of micro-organisms is always limited, and often very small—hardly ever so abundant that the simple mechanical effects of their presence can be considered as a factor in the morbid results. "We find them far more frequently in the blood at autopsies, even very fresh ones, than we are able to do during life. The pyogenic cocci, like most pathogenic bacteria, only exceptionally are able to multiply in the circulating blood of human beings. The greater frequency of their presence in demonstrable number at autopsy may be due in part to their multiplication after death, but this cannot be the sole explanation, as the cocci are found in autopsies made very early after death, more frequently than they are found during life. The explanation is probably that during the last hours of life they often find suitable conditions for their multiplication in the blood." They "grow outside of the circulating blood, and often do not make their appearance in any considerable number in the circulation until shortly before death and after the manifestation of grave constitutional symptoms."[1]

Exactly what determines the admission or exclusion of the organisms, or the mildness or severity of their effects after they gain access to the circulation, is not understood: a mere scratch with infected material from a suppurating or erysipelatous centre or a dissection wound may be followed rapidly by fatal results after but little local reaction. On the other hand, the condition of the infected tissues undoubtedly has great influence over the result, and if they permit the passage of only a few microbes, these may be destroyed without disastrous consequences by their inherent germicidal properties. The development of pathogenic organisms within the body is undoubtedly facilitated if their poisonous chemical products are absorbed at the same time with them. The septic intoxication that ensues impairs the power of resistance of the blood, bloodvessels, and tissues, and favorable opportunities are afforded for the development and reproduction of micro-organisms at distant points. "If a large quantity of pus microbes is introduced into the peritoneal cavity or directly into the circulation, death results from sepsis before a sufficient length of time has elapsed for the pus microbes to produce the histological changes which are necessary for the production of pus" (Senn). But in septic infection the intoxication is intensified and perpetuated by the microbes which have gained access to the circulation and find conditions favorable to their growth and reproduction. Thus the patient is not only poisoned by toxins formed at centres of infection, but also by those formed within the body.

Different conditions vary the activity of pathogenic organisms. Experimentally, these variations have been shown to be brought about by many modifying influences; clinically, widely different morbid results are observed to be produced by a single species of bacterium in proportion to its virulence—at one time intense septic infection, at another localized inflammation. Under inoculation pathogenic micro-organisms prove more virulent when derived from centres of infective inflammation. Welch points out the modifying influence of mixed infections upon pathological results—an influence that probably depends upon the

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[1] Welch, *Dennis's System of Surgery.*

ects of the chemical products of one bacterium upon the vitality of
other, and which may be exerted in diminishing or intensifying the
rbid processes. "A bacterium of attenuated virulence may become
ented in virulence by inoculation in combination with another
es which need not necessarily be itself pathogenic, or sometimes
ply in combination with the chemical products of another species.
se mixed infections very often occur in man." He also notes the
requency of secondary infections with pyogenic bacteria, especially
treptococcus pyogenes, in various specific infectious diseases, such as
phoid fever, tuberculosis, diphtheria, scarlet fever, smallpox, and
er affections, these increasing the conditions favorable to the de-
lopment of the purely septic micro-organisms.

At present it is not possible to offer a scientific justification of the clinical definitions of the different forms of septicæmia. Sharp limitations do not exist, and it is probable that purely saprophytic septicæmia occurs but rarely; but for practical purposes it has been found convenient and advantageous to assign to septicæmia three types. These are—

(1) A febrile reaction due to the presence in the blood of toxic substances absorbed from putrefactive or suppurative foci, where they are produced by the vital activity of bacteria, which, however, remain restricted to the sites of their original production, and do not gain access to the blood, or, reaching this fluid in limited numbers, are incapable of growth and reproduction there (septic intoxication).

(2) A febrile reaction due to the presence in the blood and tissues of toxic substances, together with the bacteria which produce them and which are pyogenic. These are derived from original foci upon the body, and after their entrance into the circulation continue to grow and to be reproduced, and to generate their toxins (septic infection; progressive septic infection).

To these may be conveniently added—

(3) A febrile reaction due to foreign aseptic substances in the blood, which determine in it the presence of fibrin ferment, which is the exciting cause of the fever. This is mild in its course and transitory (fermentation fever).

The sources of septic intoxication and septic infection are suppurative and putrefactive centres of all kinds upon the surface of the body or the mucous membranes, as well as lesions and abrasion of any kind whereby an absorbing surface is exposed to the influence of the pathogenic organisms. It is doubtful that micro-organisms can gain the circulation through the unruptured epidermis, but it is possible that the mucous membrane does not offer an impassable barrier to them. It is, of course, impossible to say what channels for their admission may not be afforded by the mucous tract, and many cases of so called "spontaneous septicæmia" originate in the infection of some undiscovered lesion. The occasional development of obscure septicæmic disorders without previous recognized injury or lesion appears to justify the claim that infection may occur through an intact membrane. Most bacteriologists at present, however, deny the occurrence of this spontaneous or cryptogenetic septicæmia.

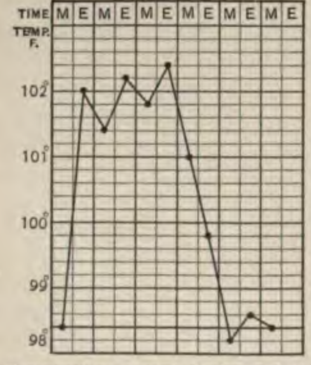
PATHOLOGICAL ANATOMY.—It is doubtful if any lesions of the tissues are produced by fermentation fever. Its course is always favorable, and the alterations it causes, if any, are transitory and have not been recognized. The morbid changes resulting from septic intoxication are never such as can be seen by the naked eye. They are microscopic and never extensive. The coagulability of the blood is certainly diminished, and putrefaction sets in earlier than is usually the case. Rigor mortis is also established early. The blood will be free of micro-organisms and of dark color. In fatal septic intoxication the course is so acute that recognizable changes in the bloodvessels and tissues will not have had time to appear. Even in septic infection (progressive) there is a notable absence of gross lesions unless the course of the disease have been protracted and septo-pyæmia have developed. After death from progressive septic infection rigor mortis occurs early.

The blood is dark and coagulates feebly or not at all. In it the micro-organisms of pus will be found often, sometimes in considerable numbers; groups of micrococci may crowd tissues and capillaries. Only slight changes may be noted at the primary centres of infection, though lymphatic vessels leading from them may be found in a state of inflammation. Thrombosis and embolism are rarely present. There may be some cloudy swelling of internal organs from superficial coagulation necrosis. There will be widespread evidence of septic inflammation of capillary vessels. A coagulation necrosis of these vessels caused by the toxins in the blood favors implantation of septic organisms, and their development and an extensive metastatic inflammation. Should the course of the septicæmia have been protracted, these foci of inflammation will have proceeded to suppuration and true metastatic abscess. Minute areas of hemorrhagic exudation from these foci of vascular inflammation are often multitudinously scattered throughout the body, and will often be found in the serous and mucous membranes and the skin. The spleen will be softened, darkened in color, and at times considerably enlarged. Effusions into the serous cavities are not infrequent. Putrefaction will be most intense in the vicinity of the original infection focus and in those parts most abundantly supplied with blood. The cadaver often exhales a peculiar putrefaction odor. Hyperæmia of the meninges of the spinal cord and brain, but no grosser lesions, will be found. The lungs will be congested and œdematous, the liver fatty, and of a dirty yellowish gray color, the hepatic venous system engorged. The kidneys are always congested, their epithelia granular and swollen. There is sometimes exudation between the glomeruli and capsules. There may be capillary extravasations into and between the tubules. Widespread catarrh of mucous surfaces will be observed; the bronchial, intestinal, renal, urinary, and uterine mucous membranes will usually present inflammatory changes and often limited areas of hemorrhage. The ovaries and uterus are often congested, and the muscular system darkened in color. The endocardium and intima of vessels will be stained by the hæmoglobin set free by the disintegration of the red blood corpuscles. Capillary extravasations are especially marked in the mucous and submucous coats of the intestines. In pure progressive septic infection pus may be found in the infection centre, and incidentally in other parts, but never as a result of the essential disorder. In many instances after protracted septicæmia metastatic abscess and pyæmic inflammations will be found, but these do not follow of necessity, and when present may be accepted as evidences of concurrent pyæmia.

SYMPTOMS.—Septicæmia and pyæmia constitute complications of medical no less than of surgical disorders. Indeed, when their origin is obscure they usually fall to the care of the physician rather than the surgeon. They are observed with great frequency as results of gangrenous and suppurative inflammations in typhoid and scarlet fevers, diphtheria, smallpox, tuberculosis, and other specific diseases. Even the analogous febrile state caused by the absorption of chemical substances formed by fermentations not bacterial in origin, *fermentation fever*, closely concerns the physician, for not only does it follow injuries, wounds, and surgical operations, but it may be excited by purely medical disorders. The transitory febrile reaction so commonly observed in childhood accompanying or following a severe indigestion presents precisely similar features, and may be attributed probably to poisonous products of abnormal fermentations in the stomach and bowels. Similarly, it is not improbable that the fevers following many hemorrhages, cerebral, pulmonary, etc., are due to absorption of ferment substances developed in the effused blood. This "fermentation fever," then, may well find a place in a work on internal medicine.

(1) *Fermentation Fever.*—Within a few, usually within twenty-four, hours after an injury, with or without external lesion, often after subcutaneous blood extravasation, after a surgical operation even so simple as the passage of a catheter, or after the ingestion of unwholesome food, the patient will develop fever with or without preceding chill. The temperature rises rapidly two, three, four, possibly six degrees (Fahrenheit). The pulse becomes full and frequent, the heart action violent. There are often flushing of the face, injection of the eyes, and throbbing headache. The tongue acquires a slight whitish coating, but remains moist. More or less complete anorexia is present, and sometimes nausea and vomiting ensue. The secretions are all diminished, the urine becoming scanty and high colored, but remaining free of albumin. The skin may be hot and dry. No especial influence is exerted upon the bowels, though constipation is often present. After rapidly attaining its maximum the fever gradually subsides, and never lasts longer than two or three days; it often ceases within twenty-four hours. (See Fig. 42.) This fever corresponds closely to that which may be induced experimentally by injecting pepsin into the circulation. In surgical practice it is said to be especially liable to occur if the superficial tissues of a wound have become necrosed as a result of antiseptic applications, or if in a closed wound extravasated blood is retained under high pressure. Headache and aching pains in the back and limbs are very common, but, as a rule, all the symptoms are mild, and frequently the thermometer alone will reveal the existence of fever. During the attack

FIG. 42.



Temperature record of fermentation fever.

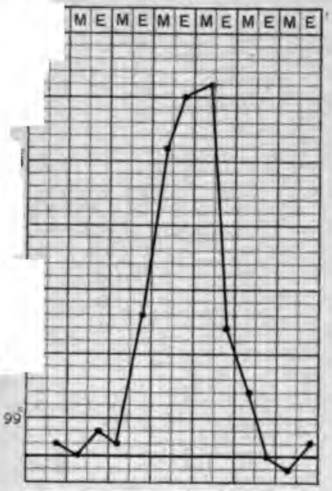
there may be, rarely, mild delirium. Examination of the blood will reveal nothing abnormal. The symptoms may subside as rapidly as they arise. No after effects are ever noted.

(2) *Septic Intoxication.*—In septic intoxication the symptoms are supposed to be due to the absorption of toxins produced at suppurative or putrefactive centres in the body by pyogenic or saprophytic micro-organisms which do not gain access to the circulation, or, at least, are incapable of growth and reproduction in it. To this form of septicæmia belongs the sapræmia of Matthews Duncan, though, as has been shown, it is very doubtful if saprophytic organisms alone are competent to exert such an important influence in septic intoxication as has been claimed for them.

Septic intoxication usually demands for its existence a centre of necrosis in the body, and the establishment of putrefaction in this. Thus it frequently depends upon the decomposition of a retained placenta, of a blood-clot, or any area of dead tissue exposed to the action of the atmosphere. The primary seat of infection will present evidences of gangrene. The surface of the slough will be dry and brownish, or will have scattered grayish, membrane-like patches. Usually a fetid odor will be exhaled. This may become intense and pervade the apartment. Many so called septic intoxications originating in purely suppurative centres are really septic infections, and indeed, in many "septic intoxications" from putrefactive centres pyogenic micro-organisms may be demonstrated. The symptoms of septic intoxication will rarely develop within twenty-four hours. They may appear later as long as any gangrenous tissue is in relation with an absorbing surface. Usually without an initial chill there is a rapid rise of temperature, which may attain 104° F. within a few hours. At other times the rise is moderate, or, again, very slight; the temperature may even fall below the normal, and this sometimes in the worst cases. The irregular temperature curves of pyæmia do not occur. The stress of the disorder is thrown upon the nervous system, but the respiratory and circulatory organs and the alimentary canal are often profoundly affected. The nervous symptoms principally consist in headache, prostration, and, later, a tendency toward narcosis and often delirium. The prostration shows itself in great muscular weakness and cardiac debility. The patient becomes indifferent to his surroundings and disposed to sleep. A low muttering delirium may appear, and in bad cases turn into coma. However, the mind often retains its clearness, even in fatal cases, almost to the end. The tongue is at first coated with yellowish white fur, but may become dry and brown. Anorexia is present; vomiting is not uncommon, and is sometimes uncontrollable. The bowels may be either constipated or relaxed. Copious diarrhœa may be present, and the stools may contain mucus and blood. The respirations become quick and shallow, but cough and intrathoracic pain are generally absent. Dyspnœa may occur from hypostatic engorgement. Jaundice is not so frequent as in septic infection and pyæmia, but the skin often has a yellowish tinge, which may be due to bile pigment or more probably to blood pigment from disintegration of red blood corpuscles. Under the microscope the red corpuscles will arrange themselves in clumps. The urine will be scanty, high colored, and acid, rarely albuminous.

cation usually develops from centres of considerable size, should the dose of toxins not be repeated the symptoms attain their acme almost at once, within a day or two if the amount absorbed have been insufficient to destroy life, or terminating in death within the same brief period should an overwhelming quantity have been received into the circulation. The disease may run a more protracted course, if the centre of absorption persist, from the repeated admission of the toxin into the blood. In this event there will be no repetition of the chill, but recrudescence of the other symptoms may be expected, varying in intensity with the extent of the intoxication, generally tending toward a fatal termination.

FIG. 43.



Temperature record of septic intoxication.

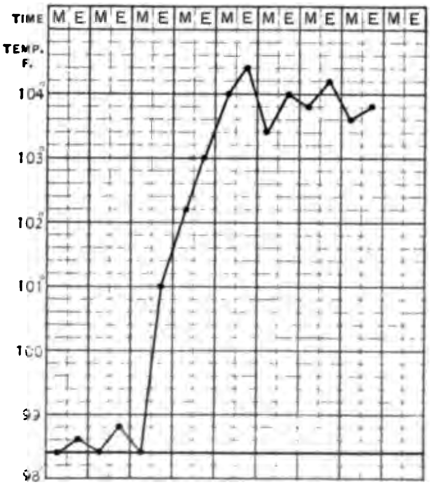
The course of septic intoxication is usually from two to four or five days. (See Fig. 43.) It rarely persists beyond the week, except in certain cases when the supply of toxin is limited and its source inaccessible, as in some examples of pulmonary gangrene, etc. Progress toward recovery is marked by a gradual subsidence of all the symptoms and the return of healthy ction in the periphery of the putrefactive focus. A fatal termination is preceded by intensification of all symptoms. The essential failure is in the nervous system. The prostration becomes extreme, the heart action feeble and rapid, and the arterial tension gradually fails. The respiration grows more shallow and hurried. The intelligence becomes more blunted ; delirium supervenes and passes into coma. The eyes are sunken, the skin bathed in sweat. Death occurs from failure of the heart.

(3) *Septic Infection* (*Progressive Septic Infection*).—While in septic intoxication the intensity depends largely upon the extent of the toxin-producing centres, this is not the case with septic infection. Here the micro-organisms are always pyogenic, more or less freely reproduced within the body, and continue to contaminate it with their freshly produced toxins. Thus we very commonly see intense infection follow a very insignificant lesion, such as a dissection wound or the prick of an infected needle or scalpel. That general infection may occur it is not at all essential that the point of original infection be in a state of suppuration or putrefaction. It is impossible to ascertain what routes for the admission of bacteria may be offered by the parts of the mucous tract inaccessible to the eye. Internal sepsis is by no means rare. Thus, septicæmia may originate from intestinal ulceration, from pulmonary cavities and suppurative centres, from empyema, from purulent pericarditis and peritonitis, from otitis media, from osteomyelitis, from pyelitis and pyelo-nephritis, and, in short, from any internal part of the body involved in suppurative inflammation. An intense and rapidly fatal sepsis follows septic peritonitis and acute multiple osteomyelitis,

while the septic symptoms from purulent pleurisy and pericarditis will be much less severe, though often more protracted. It is reasonably certain that septicæmia may develop from an urethral stricture. While the so called spontaneous septic infection cannot be allowed, the obscurity of the source of some septicæmias even suggests the entrance of micro-organisms through the intact mucous membrane.

. It is usually impossible to account for the origin of an osteomyelitis or of an ulcerative endocarditis in the absence of any demonstrable lesion; but at present it would be rash to assert that septic bacteria can reach the circulation except through some lesion of continuity. The unruptured pulmonary mucous membrane, for example, is almost certainly impervious to them, though intoxications from sewer gas by this route may readily take place. Without doubt, pyogenic organisms in limited numbers may enter the circulation, and, not finding conditions favorable to their development, perish, or at least remain quiescent so long as the blood and tissues maintain their normal powers of resistance. On the other hand, especial virulence may destroy life so speedily that time will not have been allowed for the production of anatomical changes; but in other and more protracted instances the organisms may only find favorable opportunities for growth in special structures, such as the bones, the endocardium, etc. Again, the toxins absorbed from primary centres of suppuration may so empoison the blood and the intima of bloodvessels that the powers of resistance of these is diminished to the degree that they come to afford the conditions for bacterial development. It is thus that in ordinary cases of septic infection colonies of micro-organisms will be found in scattered foci of the capillary system, and when life has been sufficiently prolonged the results of their activity may even be thrombosis and embolism and pyæmic abscess.

FIG. 44.



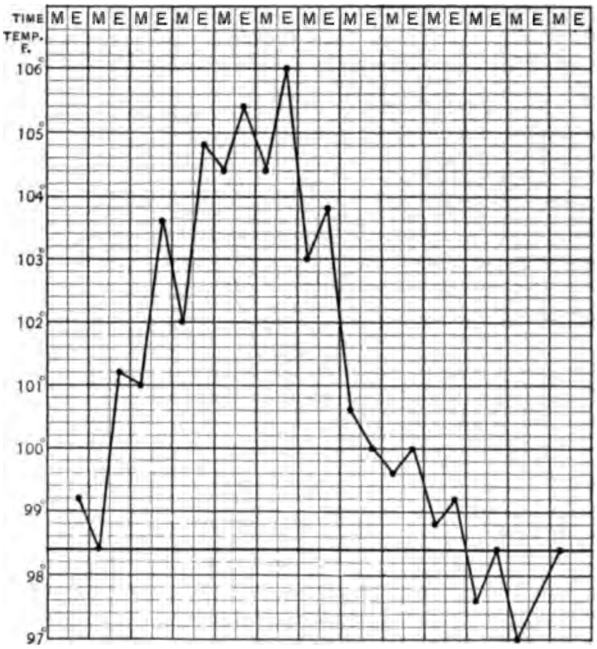
Temperature record of septic infection.

The symptoms of septic infection rarely begin within twenty-four hours, usually only after three or four days. There may be an initial chill; more commonly there are only chilly or "creepy" sensations. Unlike septic intoxication, septic infection does not reach its maximum tensity immediately after the onset. (See Fig. 44.) The fever gathers rce as the micro-organisms develop and produce their toxin. The course of the established disease is that of a septic intoxication. In some cases, even in those pursuing a rapidly fatal course, there may be but little elevation of temperature. Generally, however, the fever rapidly attains a height of 102°–104° F. The latter temperature is not often exceeded, even in fatal cases. Slight morning remissions are often observed. The pulse is notably of low tension, and may be very frequent, 120–140 or more to the minute. Microscopic examination of the blood rarely reveals the presence of bacteria, but will show sometimes marked leucocytosis with decided diminution in the number of red corpuscles. The nervous symptoms quickly appear, and the patient develops a remarkable indifference to his surroundings and his danger. Little or no agitation or jactitation will be exhibited. There is rather a profound depression of muscular activity. The mental indifference is often accompanied by persistent somnolence and succeeded by low muttering delirium. The tongue, at first moist and coated, as the disease advances becomes reddened at the tip and border, but often dry and brown, almost black, at the centre. There are great thirst and complete loss of appetite. Nausea and vomiting are frequent, as is diarrhœa. Later the stools may become bloody, and sometimes pronounced entero-colitis results. The skin assumes an earthy color. This often passes into a slight icteroid hue, which is attributable rather to liberation of blood pigment than to hepatogenous changes. Toward the conclusion of fatal cases it may be bathed in sweat. Sweating is frequent in all cases; it may be intermittent. Various cutaneous eruptions are often observed. These are usually erythematous. They may be distinctly scarlatinoid in character. Most cases of so called surgical scarlatina are really septic. This eruption often begins in the vicinity of the original focus of infection, but may show itself upon any part of the surface. It rarely shows the diffuse characters of true scarlet fever. The erythema may also be distinctly erysipeloid, but differs from erysipelas in being painless. Usually the erythema is in scattered patches. Vesicular and pustular eruptions are also occasionally observed. In fatal cases petechiæ, sometimes in large numbers, and ecchymotic extravasations of blood, appear upon the skin.

The urine is scanty, of high specific gravity, loaded with urates, but usually free from albumin. The primary seat of infection becomes dry and inactive, and in severe cases very foul. In puerperal septicæmia the lochia become offensive in odor, and are diminished or even suppressed. (In favorable cases the primary lesion gradually acquires a healthy appearance or a re-establishment of the lochia takes place.) The secretion of milk diminishes or is suppressed. During the course of the disease fresh absorption of infective material may be marked by recurring chills, but these are never so pronounced or frequent as in pyæmia, nor are the variations of temperature so decided as in this disease. In milder and favorable cases, though the temperature may be high, the pulse retains some volume, and its frequency may not exceed 80 to 90.

The lymphatic system is always involved in septic infection. Upon the skin the path of invasion may often be traced by a red line corresponding to the inflamed lymphatics leading from the point of infection. The lymphatic glands nearest to the infective centre are often much enlarged and very tender. A general adenopathy may sometimes be developed. The spleen is always enlarged and its percussion area increased. Sometimes it may be discovered by palpation. Some cough may be present. It is generally dependent upon bronchitis. Pneumonia is not a common complication of septicæmia. Occasionally a considerable degree of hypostatic engorgement of the lungs will be encountered. In favorable cases of septic infection improvement is first noted in a lowering of the temperature and increased tension and diminished frequency of the pulse. In fatal cases death approaches as in septic intoxication, with increasing asthenia, failing heart, delirium, and coma, though a fair degree of intelligence may be preserved until near the end. It may occur within twenty-four hours; usually it is not delayed beyond the week.

FIG. 45.



Temperature record of septic infection.

Carbuncular inflammation is often a cause of even fatal septicæmia, probably of infective nature, but it is impossible to decide whether we should consider as septic infections or septic intoxications those milder febrile reactions that so often accompany the development of a furuncle or small abscess and similar processes. Usually the general symptoms promptly subside with the amelioration of the suppurative centres, but occasionally fatal septicæmia and even pyæmia result.

A most important consideration is the septic infection that so often ms a factor in the course of various specific disorders, such as scarlet er with severe angina, smallpox in the maturation fever, typhoid r, diphtheria, tuberculosis, etc. This is nearly always a streptococ- infection, occurring through the peculiar lesions of these diseases, in many cases constituting the essential cause of death. Important hese secondary infections must be, it is most difficult for the physi- to determine the extent to which they are responsible for the esults, as distinguished from those of the primary infections. It is asonably certain that the enormous streptococcus invasion of the ature eruption of smallpox largely influences the outcome of this affec- n. Similarly in scarlet fever and diphtheria the abundant presence streptococci and staphylococci in the faucial membrane affords the rest possible opportunity for the concurrent development of septicæ- ia. In the former affection especially the suppurative complications nd sequels even in remote parts of the body conclusively prove the admission of pyogenic organisms to the circulation. It is well known that the hectic fevers of advanced tuberculosis are principally due to septic intoxication following the invasion of softened tuberculous foci by pyogenic bacteria. Probably the most interesting secondary septicæmias are those complicating and following typhoid fever. (Though the typhoid bacillus is itself pyogenic, and may be found occasionally as a pure culture in post-typhoid pus formation, it is likely that the great majority of these inflammations are dependent upon the commoner pus bacteria. After the third or fourth week of this fever typhoid bacilli are discovered only with difficulty, and the prevailing bacteria found in localized inflammations are streptococci.[1]) It is not impossible that many unduly protracted cases of typhoid fever, and even of supposed relapse, are really septicæmic.

The most obscure septicæmias are those that have been called cryptogenetic, from the supposed passage of pyogenic bacteria through a healthy or intact mucous membrane. Such cases, in fact, probably always originiate in some undiscovered primary focus: the root of a carious tooth, the middle ear, a nasal sinus, an urethral stricture, or any minute lesion of the mucous tract (Welch) may be the starting point These infections often result in a more chronic septicæmia, lasting often several weeks, and often enough running a mild course. In chronic septicæmia there are often developed recognizable centres of local inflammation; mild endocarditis, pleuritis, pericarditis may arise. There may be also pulmonary engorgement and œdema and pronounced enteritis. Apart from puerperal and ordinary surgical septic infection, there can be no doubt that many septicæmias of feeble intensity and of favorable course are encountered, especially by the physician, and are accountable for many unduly protracted and not understood febrile processes. Chronic septicæmia of greater potency may not only develop localized inflammations, as has been shown, but may result in pronounced pyæmia. The micro-organisms of septic infection and of pyæmia are the same.

DIAGNOSIS.—Fermentation fever ends at a time when septic intoxication and septic infection begin: within a few hours after its exciting cause it begins, and within a day or two it terminates. Its uniformly favorable course will serve to distinguish it. It is impossible to draw a sharp distinction between septic intoxication and septic infection; it is not even certain that such exists. Septic intoxication can usually be traced to a putrefactive centre, a slough or a decomposing retained placenta or a blood clot, which announces itself by a strongly putrefactive odor. It usually does not appear earlier than twenty-four hours after the establishment of putrefaction, sometimes not earlier than several days. It acquires its acme almost at once, and its intensity depends upon the quantity of toxine absorbed. Removal or destruction of the putrefying tissues will be followed at once by a subsidence of the symptoms, provided a lethal dose of the toxin has not been absorbed already. Septic infection also requires time for its development after inoculation, and its symptoms increase in intensity as the bacteria increase in the body. Absence of putrefaction and the appearance of septicæmic symptoms after a slight or not extensive injury, or the occurrence of suppuration, would indicate septic infection, though it should not be forgotten that septic infection may also arise from a putrefactive focus. It may be extremely difficult to distinguish between milder and more protracted forms of septicæmia from typhoid fever; indeed, during the latter part of this disorder and while the intestinal ulcers are unhealed a septic infection often occurs and a state of mixed infection is created. So called recrudescences and relapses of typhoid fever are often examples of pure septic infection in which a typhoid element may no longer exist. During the early stage of typhoid fever the diagnosis may generally be made after a few days—by recognition of essential typhoid symptoms on the one hand, and on the other by the absence of a primary infective focus. Internal sepsis, however, very frequently offers great difficulties of diagnosis, and only the most careful observation and comparison of symptoms will protect from error.

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[1] Dunin, *Archiv für klin. Med.*, Bd. 39, S. 369.

The microscope will reveal the presence of the plasmodium in the blood in malarial fever. But in default of these means of differentiating the greatest difficulty often exists, and the presence or absence of chronic septic infection can only be determined at times by the development of local inflammatory lesions, or even of the evidences of local suppurations characteristic of pyæmia. The septic infection of multiple acute osteomyelitis may be determined after careful examination of the osseous structures. A rash is sometimes seen in septicæmia which may resemble that of scarlatina or rubella. This is generally circumscribed, and follows a course quite unlike that of these affections. In pyelo-nephritis and tubercular disease of the kidney, as of other organs, the febrile reaction is probably the result of a mild septic infection.

As a rule, however, the diagnosis of septicæmia is not a matter of difficulty, since in most cases there is a clear history of a wound or surgical operation or of an infective inflammation or of an abortion or delivery. Much greater difficulty will exist when the source of infection remains undiscovered. In such cases the symptoms are often sufficiently characteristic, but frequently the diagnosis can only be made by exclusion.

Septicæmia should always be suspected during the course of any disorder the lesions of which afford any opportunity for the growth and development of septic micro-organisms, when the symptoms of that disorder depart from the usual type and an elevated temperature continues beyond the usual duration.

PROGNOSIS.—Fermentation fever always pursues a mild and favorable course. Septic intoxication is always dangerous, but its termination depends upon the amount of toxin absorbed. Generally, the greater the area and intensity of the primary putrefaction the more surely will the end be fatal. A septic intoxication may destroy life within twelve hours. Septic intoxication from progressive gangrene is generally fatal. The prognosis is much more favorable if the primary focus is limited in extent, and so situated that it may be removed or destroyed; otherwise the continuous absorption of toxin, even from areas of limited extent, may cause death. A favorable prognosis is justifiable if, after the original intoxication, the source of supply be destroyed and the graver symptoms not manifested. Increased frequency of the pulse with constantly lowering arterial tension, the occurrence of delirium and coma, increasing depression, extravasation of blood, are all signs of approaching death. Progressive sepsis or septic infection is generally fatal. The prognosis cannot be determined from the condition or extent of the primary infective focus. Rapidly fatal septicæmia may depend upon a slight scratch or abrasion, and the result is determined by the virulence of the organisms, the numbers in which they enter the circulation, and the degree of resistance offered by the blood and tissues of the individual. Other things being equal, however, the introduction of large numbers of infective micro-organisms to the blood, which find conditions favorable to their growth, renders recovery almost hopeless. The presence of more than one infective centre greatly increases the gravity of the case. Internal sepsis is also very fatal, though often very protracted in its course. The probabilities of recovery will be increased by destruction of the activity of the primary centres of infection. The occurrence of subcutaneous hemorrhage almost certainly presages approaching dissolution. Delirium, coma, increasing debility of the cardiac and general muscular systems, are most unfavorable signs. A favorable prognosis may usually be made in the milder sepsis that accompanies the course of boils, carbuncles, small abscesses, and that occurs as a sequel to typhoid and scarlet fevers. The septic symptoms that arise in the course of purulent inflammation of serous membranes will usually subside if successful surgical treatment corrects the suppurative focus.

TREATMENT.—Fermentative fever requires no treatment: with the removal of its exciting cause it subsides spontaneously and speedily. For septic intoxication and septic infection there are no specific remedies or methods of treatment. In septic intoxication the most important therapeutic indication is to disinfect the putrefactive or suppurative centre whence the toxins have been absorbed. The removal of gangrenous masses by surgical measures and the arrest of progressive gangrenous processes by cauterization and other appropriate means, the thorough sterilization of centres of putrefaction and suppuration, will ensure the recovery of the patient, provided a fatal dose of toxin have not been absorbed previously. Surgical measures for the prevention of coagula which may become putrid, and the removal of these when formed, the removal of putrefying portions of placenta or of blood clot from the uterine and vaginal cavities, and subsequent disinfection of these by irrigation and the use of antiseptic agents, are best detailed in works upon surgery and obstetrics. The efficient performance of such treatment is often followed by the most gratifying results. Even within a few hours the temperature falls, the pulse becomes fuller and slower, the nervous symptoms disappear, and the patient enters at once upon convalescence.

In combating the effects of the poison already absorbed all hope of specific treatment should be abandoned. The sole object should be to support the vital powers against the profound depression that involves them. The use of internal antipyretics it never justifiable. The reduction of febrile temperature brought about by them never compensates for the increased danger of further enfeebling the already depressed heart action. It is not so certain that quinine may not exert a favorable influence, not simply as an antipyretic, but possibly through some specific action upon microbes and as checking tissue metamorphosis. In reasonable doses it does not depress the nervous system as do the coal tar derivatives. Daily doses of from twenty to thirty grains often seem to be beneficial. If the range of temperature be high, positive benefit will often follow cold water sponging or bathing. The reduction of temperature thus secured is at the cost of no depression of the nervous system; indeed, a tonic influence upon this system may often be noted in the slower and fuller pulse, the cleansing of the tongue, and the diminution of delirium. Intense headache may be relieved by the ice cap. To support the failing heart is a most important indication. To this end strychnine, digitalis, strophanthus, and belladonna are the most valuable drugs. Digitalis and strophanthus too often impair appetite and digestion, and even excite nausea and vomiting; moreover, their value as heart tonics is greatly less in febrile than in afebrile conditions. Strychnine is far preferable to all other heart tonics and stimulants, and often affords remarkable benefit; from one twenty-fifth to one fiftieth grain of the sulphate may be given every fourth hour, hypodermically, for days at a time. Concurrently, small doses of belladonna (from one to three minims of the fluid extract) or of atropine sulphate (from one ninetieth to one hundred and fiftieth of a grain) may be administered. Alcoholic stimulation is nearly always advantageous. In severe cases the quantity of brandy or whiskey that can be taken with apparent advantage is sometimes enormous. As much as a quart of whiskey has been given during the twenty four hours to patients who have recovered. Pronounced flushing of the face affords a guide for limiting the supply of alcoholic fluids. Ordinarily, from a half ounce to an ounce of brandy or whiskey may be given every second hour. Evidence of the favorable action of these agents will be an improved tone and diminished frequency of cardiac pulsations, a lowered temperature, and an amelioration of nervous symptoms. From one to five grains of ammonium carbonate may be given alternately with the alcoholic stimulant. The use of opium is rarely called for in septicæmia, except when diarrhœa or entero-colitis becomes troublesome; then small doses are often useful: a fluidrachm of the camphorated tincture of opium, with twenty grains of bismuth subnitrate, given every third or fourth hour, will usually suffice to hold these symptoms in check.

When the primary infection centre is in the alimentary canal, as m typhoid or dysenteric ulceration, intestinal antisepsis should be npted. The best drugs for this purpose are napthaline and salol. n sixty to eighty grains of either of these would be a daily dose. mild degrees of intestinal sepsis this treatment may do good; the ls can certainly be deodorized, but it is unlikely that any remark- e antisepsis can be exerted by so small an amount of disinfectant n so great a surface.

The medical treatment of septic intoxication and septic infection is same. Equally in the two forms the only specific treatment is sur- , whereby the foci of putrefaction and suppuration are destroyed eprived of their power to intoxicate or infect. Internal medication nds upon supporting remedies and nutrition. In chronic septicæ- the result will largely depend upon the support thus given. The t in all cases should be simple and almost exclusively liquid. If it e possible to limit the patient to a milk diet, nothing better could be ished. From three pints to a half gallon of skimmed milk will be ample for the twenty four hours. This may be given in quantities of a half pint every three hours or in smaller amounts at shorter intervals, as the case may require. Strong beef or other animal broths or soups may alternate with the milk. Eggs, boiled or poached or beaten up with milk or water, are often acceptable, and will be readily borne by the stomach. It is better to give rather too little than too much nourishment. In the latter case gastric distress, nausea, and vomiting may be excited. During convalescence iron preparations with bitter tonics will be indicated.

SMALLPOX AND VARIOLOID.

BY WILLIAM M. WELCH, M. D.

SMALLPOX.

SYNONYMS.—Latin, Variola; French, Petite-vérole; German, Blättern or Pocken; Italian, Vajuolo.

DEFINITION.—Smallpox is an acute infectious disease, characterized by an initial fever of about three days' duration, succeeded by an eruption passing through the stages of papule, vesicle, and pustule, ending in incrustation, and leaving pits or scars; the fever either intermitting or remitting in the papular and increasing in the pustular stage.

HISTORY.—There is no doubt that smallpox was known for several centuries before it was described. The credit of having first described the disease is generally given to Rhazes, an Arabian physician who lived in the early part of the tenth century. This physician, however, ascribes to Galen and others before his time a knowledge of the disease, although they failed to give an intelligent account of it. According to Gregory, the word *variola* appears in several Latin manuscripts preserved in the British Museum and bearing date considerably prior to the year 900, thus proving that the disease was known before Rhazes called attention to it.

The term "variola" is probably derived from the Latin word *varius* (variegated or spotted), while the term "pock" is of Saxon origin and signifies a bag or pouch. To the latter term was prefixed the English word *small* or the French word *petite* somewhere about the year 1500, in order to designate this disease from syphilis, which was sometimes called the great- or grandpox.

From the East smallpox extended to other parts of the world, following, doubtless, the lines of travel and commercial intercourse. It appears to have reached England in the latter part of the ninth century. Soon after the discovery of America the scourge was introduced on this continent. It first appeared in Mexico in 1520, having been brought there by a negro slave, and thence it spread over the whole of this vast country, decimating in many instances large settlements of Indians. Multitudes of these people were swept away by the disease when it first appeared in Massachusetts in 1633. It reached Boston in 1649, and subsequently prevailed there or in that vicinity in epidemic form every few years.

In almost every country on the globe smallpox long constituted one of the most dangerous and dreaded diseases to which mankind was subject. It was present in one place or another almost constantly, and frequently prevailed with great malignancy over vast tracts of territory, claiming as its victims persons of all ages and from every station of life.

t only the number of deaths, but the marred visages of persons in ry community, testified to the frequency of the disease. Indeed, it so prevalent in the Middle Ages as to lead to the common saying "From smallpox and love but few remain free."

inoculation period, or the time when the practice prevailed of ating the variolous poison, constitutes an interesting epoch in the ory of smallpox. This practice was based upon the well known fact t the disease very rarely occurs more than once in the same individual; hence the advantage of producing in this way a possibly milder of the disease.

Inoculation was undoubtedly practised in China and India at a very te period, though in a very crude manner. Thence it gradually nded to Asia, but it does not appear to have been used very intellintly or scientifically until it reached Constantinople, about the year 700. The method was introduced into England by Lady Mary Worty Montague, who, after satisfying herself of its advantages, subjected r two children—a son and daughter—to the new process. The son as sent to Constantinople in 1717 to be inoculated, and, the result proving satisfactory, the daughter was inoculated in England in 1721. There was at first violent opposition to the method, both on the part of physicians and the clergy, yet, mainly through the influence and example of this woman, it was very soon brought into widespread esteem.

From England the novelty travelled rapidly to most other countries, reaching America the same year (1721). It was introduced into this country, at the suggestion of the Rev. Cotton Mather, by Dr. Zabdiel Boylston of Boston, who first inoculated his only son, about thirteen years of age, and two negro servants. Before the practice was generally accepted, however, it was necessary to overcome here, as in England, much violent opposition.

The principal advantage claimed for inoculation was that smallpox thus produced was much milder in type than when the infection was received in the natural way. While the death rate from natural smallpox was one out of every three or four persons attacked, it was, at the highest, from the inoculated disease, not greater than one out of fifty, and sometimes as low as one out of two hundred—the average death rate being somewhere between the two. The disadvantage was that smallpox produced in this manner, although milder in type, was just as contagious as when contracted naturally; hence inoculation had the effect of keeping the disease almost constantly in existence, and the annual number of deaths from the disease was even greater than prior to its introduction.

Inoculation was practised for nearly a century, when it was superseded by Jenner's discovery. Vaccination was soon found to possess all the merits of the former, without partaking of any of its objectionable features, and hence its greater claim for preferment. The introduction of vaccination may be said to have brought about a great change in the history of variola. Instead of being the widespread and fatal disease of former times, smallpox prevails today with frequency and intensity only in countries and communities where this eminently protective agent is refused or neglected.

ETIOLOGY.—The spread of smallpox to nearly all countries of the globe shows that conditions of soil or climate exert no influence over the disease. It prevails wherever predisposed individuals are exposed to the infection. But few can boast of natural immunity from the disease. This individual peculiarity is occasionally met with, as may be seen by reference to the history of the disease during the pre-vaccination period. Persons have been known to go through life constantly exposed to the infection without suffering from any of the manifestations of smallpox. It is said that Morgagne, Boerhaave, and Diemerbroek could boast of this peculiarity. Yet instances are recorded where persons have resisted the infection when received in the natural way, but have yielded to the disease late in life by inoculation. Gregory gives an example of this kind in the case of a lady who brought up a large family of children, many of whom she nursed through smallpox without receiving the infection herself, but at the age of eighty-three she took the disease by inoculation. While but few are naturally insusceptible to smallpox, yet at the present day, through the agency of vaccination, individual susceptibility is greatly changed, and even absolute immunity is enjoyed by the greater part of the population.

Sex.—The predisposition to smallpox is certainly not influenced by sex. Under the same conditions males and females are equally susceptible to the disease.

Race.—As to whether race exerts any influence there is some difference of opinion. Most authors, however, agree that the predisposition is more marked among the dark skinned races, particularly the negro race. There is no doubt that when smallpox prevails epidemically in this country the proportion of deaths to the cases is greater among the negro than the white race; but this, I believe, is owing to the fact that there is greater neglect of vaccination by the former. In my experience the unvaccinated cases of each race have perished in about the same proportion.

Age cannot be said to influence the predisposition to the disease, as it is naturally present at all periods of life from earliest infancy to extreme old age. If aged persons are found less susceptible at all, it is because of the prophylactic power of vaccination. While nursing infants under six months old commonly resist the infection of measles and scarlet fever, they are quite sure to yield to the infection of smallpox. Even the fœtus *in utero* is not exempt from the danger of an attack when a pregnant woman suffers from the disease. The variolous process in such a patient is exceedingly liable to excite abortion or premature delivery, and the fœtus or child may show evidence of the disease in the form of local lesions. Such evidence has been observed as early as the fourth month of fœtal life, and at various periods thereafter until the completion of gestation. I can recall in my experience at least one case in which the child was born at the eighth month with the variolous eruption just appearing. The eruption was confluent, and death occurred during the suppurative stage.

In the majority of cases of infection of the fœtus it is found that it does not pass through the disease coincidently with the mother, but at a somewhat later period. It would appear, therefore, that infection in its case does not occur until the mother manifests symptoms of the disease, and that its case is marked by a distinct and separate incubation period. When we consider the close relationship of the blood of mother and fœtus, this seems remarkable, but not more so than the fact that the fœtus frequently escapes infection altogether. Very often, indeed, the pregnant woman passes through an attack of smallpox without abortion occurring, and when the child is born at full term it is found to have the usual susceptibility to variola or vaccinia. I have vaccinated a considerable number of infants born under such circumstances, and have seldom if ever failed to produce in them the vaccine disease. Very exceptionally, however, a child survives an intra-uterine attack of variola: such a child when born may or may not show scars, but is, of course, insusceptible to vaccinia.

It is well known that a pregnant woman while personally immune from smallpox is liable to miscarry when exposed to the infection of the disease. In consequence of such exposure during the latter stage of pregnancy healthy mothers are said to have given birth to infants affected with variola. While the possibility of such an occurrence cannot be excluded, yet it seems to me that the more probable explanation in such cases is that the mother had suffered from *variola sine exanthemata*—a form of the disease most likely to pass unrecognized. A child thus infected *in utero* and recovering from the disease might be found at birth and ever afterward insusceptible to variola. It is not impossible that some of those, like Diemerbroek and others, who claimed for themselves natural insusceptibility to the disease may have acquired immunity in this way.

Infrequent instances are met with of apparently healthy persons resisting the infection of smallpox at one time and yielding to it at another. I will relate a case in point: In 1874 a colored man, aged thirty, came under my care suffering from confluent variola. He stated that vaccination had been performed at different times during his life, but never successfully. In 1871 he belonged to the crew of a sailing vessel on which several cases of smallpox occurred, and his duties required him to come frequently in quite close contact with those who were ill, yet he did not take the disease. He was vaccinated at the time, but, as before, without result. When he fell ill with variola three years later he was unable to account for the source of the infection. The attack proved fatal. Not only cases like this, but those cited when considering the history of smallpox inoculation, show that susceptibility to the disease may occasionally, from some unknown cause, be temporarily absent. Experience also shows that the susceptibility may at one time be diminished, and at another greatly increased.

The existence of acute and chronic diseases is said by some to lessen temporarily the susceptibility to the infection of variola. Curschmann believes that it is very slight among patients while in the acute stage of scarlet fever, measles, or typhoid fever. Several patients of his while suffering from the latter disease were exposed to the contagium of smallpox, but infection, he thinks, did not occur in any case until the body temperature became permanently normal. He was led to this conclusion from the fact that the interval between the time when the temperature reached the normal point and the beginning of the initial stage of variola corresponded to the longest period of incubation of the disease that is met with—namely, fourteen to nineteen days. There is no doubt, however, that variolous infection does frequently occur during the existence of an acute disease, and that the incubation period in such case is often greatly prolonged; and, furthermore, that smallpox has been known to coexist with almost every form of chronic disease—with typhoid fever and the acute exanthemata, especially scarlet fever and measles. I have seen unprotected children, while suffering from measles in its most acute stage, exposed not longer than two minutes to the infection of variola, sicken with the disease after the usual incubation period. Also, I have seen, in one instance at least, smallpox coexist with scarlet fever, and quite frequently with syphilis in its various stages.

The susceptibility to smallpox is removed by vaccination, but frequently reappears to a greater or less degree in a variable period of time. So also one attack of smallpox does not invariably protect the individual for the remainder of life against a future attack. It is undoubtedly the rule that a person does not suffer from the disease more than once, but quite well authenticated cases of second attacks are recorded. Indeed, some writers allege that the predisposition to smallpox in some persons is so strongly marked as to render them susceptible to the infection more than twice, even as often as five or six times. The authenticity of reported cases of this kind, however, is not to be taken for granted, but accepted with extreme caution, as there are so many sources of error.

As to the frequency of secondary or recurrent smallpox, there is some difference of opinion on the part of authors. Some of the more practical of those who wrote in the early part of the last century hesitated very long before believing that it was possible for the disease to recur. It was estimated at that time that among ten thousand cases of smallpox not more than one or two were genuine recurrent cases. The infrequency of such cases was also noticed during the inoculation period. Jenner, who closely studied both casual and inoculated variola for more than thirty years, was very positive in his views as to the permanency of the protection which one attack of the disease confers, and it was doubtless his positive convictions on this point that led him to announce his over-sanguine belief in the never-failing efficacy of vaccination. Gregory, who enjoyed unusual opportunities for studying variola, was very incredulous on the subject of recurrence of the disease. Most of the reported cases which he was called upon to examine he found incorrectly reported. Ecthyma, pustular syphilis, and particularly varicella, he states, were fruitful sources of error. But few patients claiming to have had smallpox previously came under his care as physician to the Smallpox Hospital of London for more than twenty years, and of these few only a very small fraction could stand the test of rigid scrutiny. In regard to the historic case, frequently quoted, of Louis XV., king of France, who is said to have died of smallpox at the age of sixty-four, after having previously suffered from the disease when fourteen years of age, Gregory says that he took much pains to investigate this case, inquiring particularly into dates, the course and duration of the eruption, and came to the conclusion that His Majesty did not have smallpox in early life, but that the disease from which he then suffered was varicella.

It is rare indeed that a physician is able to say that he himself has seen two distinct attacks of smallpox in the same individual: the evidence relied upon to prove the occurrence of second attacks is usually obtained from the patients themselves. To accept without question their statements on this point would, I am sure, be very misleading. I have seen in the hospital a number of patients who claimed to have had smallpox previously, but only a very few were able to show anything like characteristic pitting; and all of those who did show such evidence of a previous attack had the disease the second time in the mildest possible form—so mild, indeed, as to be scarcely recognizable, the eruption being either simply papular or barely vesicular. I have never seen an unmodified, or even a severe, case of smallpox occur in a person who was deeply and characteristically pitted from a previous attack. Nor has any person during the last quarter of a century been admitted to the Philadelphia Municipal Hospital twice suffering from the disease. In view of these facts it seems probable that second attacks of smallpox are much rarer than is generally supposed.

The cause of smallpox doubtless resides in a specific micro-organism. As pathogenic microbes have been found in a number of contagious diseases, it is evident that such a microbe must exist in a disease so typically infectious as smallpox, although it has not yet been described. The only micro-organisms thus far discovered are such as belong to suppurative processes. For example, there have been found in the pustules the *streptococcus pyogenes*, and in cultures from the pustules the *staphylococcus pyogenes aureus* and *staphylococcus albus*. The bacteriological study of the disease is therefore incomplete.

But, while we are not yet positively informed as to the bacteriology of smallpox, there is no doubt that the disease is spread by means of a specific virus which is reproduced in every patient. That the infecting principle is contained in the pustules has been clearly proved by smallpox inoculation. It is also contained in the exhalations from the body, in the breath, and probably in the various secretions, although this has not been demonstrated. Zülzer proved that it is contained in the blood by successfully inoculating a monkey with blood taken from a smallpox patient.

The contagium emitted by a patient is most intense in his immediate vicinity, but it may be transported in an active state for some distance by the atmosphere. It is impossible to fix definitely the striking-distance of the contagium, since this depends largely upon the number and severity of the cases collected together. If a susceptible person should enter a small apartment containing one or more severe cases of smallpox, infection would almost certainly occur, while if the apartment be large and well ventilated and the cases few and mild, the risk of infection would be greatly diminished, or if he should approach equally near the same cases in the open air, the risk would be still less.

Smallpox is undoubtedly infectious in all stages characterized by symptoms. It is alleged by some that the disease is even infectious during the incubation period, but I think there is very little reason to believe that such is the case. It is not improbable, however, that the blood of a person in this stage of the disease might convey the infection if it were introduced into the veins of a susceptible individual. An interesting case is reported by Schaper, showing that the infection was transmitted during this stage by skin-grafting. The small pieces of skin used for the purpose were taken from a person who several hours later began to manifest symptoms of smallpox, and the individual upon whom this skin was transplanted was attacked by the disease on the sixth day after the operation.[1]

Excepting the incubation period, the disease is least infectious during the initial stage, and most highly so during the suppurative and early period of the desiccative stages. The scabs are unquestionably infectious, and as long as these remain on the skin the patient should be regarded as dangerous to the community. Even after death the body still retains the power of transmitting the contagium. This fact has been demonstrated more than once where public funerals have not been interdicted, and where the bodies of persons who have died from smallpox have by accident found their way into dissecting rooms.

While the contagium of smallpox is perhaps more commonly conveyed from person to person through the atmosphere, yet this is not the only medium of infection. The infecting germs become attached to all objects in the immediate vicinity of the patient and cling to them for a variable length of time. Objects which have a rough, shaggy surface, such as blankets, woollen clothing, etc., not only become more intensely infected, but hold the infection much longer, than smooth objects. Woollen garments closely packed and excluded from the air as completely as possible have been known to retain the infection for many months, and even years. If, however, such garments be freely exposed to the atmosphere and sunlight, the contagium will soon be destroyed. Of course it may be destroyed at once by disinfecting agents.

Not only objects in the room of the patient, but also healthy persons whose duties require them to come in contact with the sick, may be the means of communicating the infection. The infection may adhere to the hands and other parts of the body of the attendants, but the chief danger is from their clothing. Great caution should therefore be observed by physicians, nurses, and others in attendance upon smallpox patients.

The manner in which the contagium enters the system is usually by absorption in the respiratory tract. When there is susceptibility to smallpox a single inspiration of air containing the germs of the disease is quite sufficient to ensure infection of the individual. While it is possible for the contagium to be absorbed by the mucous membrane in the upper part of the air passage, there is no doubt that absorption takes place principally through the lungs. It is well known that the contagium never enters the circulation through the skin, except by inoculation. The older writers believed that it was possible for the virus to enter by the mucous membrane of the alimentary canal, especially by the stomach, but the comparatively recent experiments of Zülzer on a monkey which was forced to swallow smallpox crusts were followed by negative results.

Conditions seem to exist at times more favorable to the spread of smallpox than at others. For instance, at one time the disease is met with in isolated cases, and shows but little disposition to spread, or if it spreads and assumes the proportion of an epidemic, the epidemic is small and marked by unusual mildness. At another time the disease rapidly spreads from a single case, and speedily assumes the dimensions and fatality of an extensive and malignant epidemic. This variation in the behavior of the disease at different times has never been satisfactorily explained. To say, as the earlier writers were wont to do, that it is owing to some peculiar condition of the atmosphere is no solution of the problem. Perhaps Diemerbroek was not far wrong when he expressed the belief that "this is one of those mysteries which nature for ever intends to keep to herself."

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[1] Curschmann in *v. Ziemssen's Cyclopædia of the Practice of Medicine.*

There is, however, one cause well understood which at the present day influences to a great extent the recurrence of epidemics, and that is the neglect of vaccination. During the prevalence of smallpox this important agent is freely employed and serves as a powerful factor in extinguishing the epidemic. But it is well known that in the course of a few years the susceptibility of very many of those previously protected by vaccination becomes gradually re-established. If we consider the large number of susceptible persons belonging to this class, together with the number of those who are apt to neglect vaccination, we can readily see how there is provided from time to time a suitable soil into which only a few smallpox germs need be introduced to give rise to an epidemic of the disease.

PATHOLOGICAL ANATOMY.—While it is generally conceded that the etiology of smallpox must be explained by the germ theory, yet nothing is known of the nature of the specific micro-organisms believed to be present in the disease, nor of their manner of attacking the blood and tissues of the body. The only bacteria described are those belonging to the cocci group, especially such as are peculiar to pus formation, but they can scarcely be said to bear a causative relation to the pathological processes of the disease.

The Skin.—The earliest, and indeed the chief, anatomical changes met with are found in the skin. Usually on the third day of the disease the characteristic cutaneous lesions begin in the form of small red spots. These are produced by circumscribed hyperæmia of the papillæ and extend deeply into the skin. Papulæ are thus formed, and as they advance in their development the epithelial cells above the congested papillæ, through an increase of protoplasm, become enlarged and granular. This distinctly granular condition of the involved epithelia causes the papules to assume at quite an early stage a solid, dense character.

The papulæ are next converted into vesicles by an exudation of lymph from the papillary layer. As the lymph increases the altered cells over the engorged papillæ are separated and changed, so as to form septa or partition walls, which give to each vesicle a reticulated or many celled cavity. While the contents of the vesicles at first is principally lymph, together with coagulated fibrin and granular matter, eventually pus corpuscles are formed, mainly by the transformation of epithelia.

Quite early in the vesicular process a depression, known as "umbilication," is seen in the centre of very many of the vesicles. This is believed to be due either to the hair follicles or the excretory ducts of sweat glands, as in either case the epidermis dips downward and forms a part of their anatomical structure. If, for instance, a vesicle forms about a hair follicle, the centre of its epidermic covering will be held down by the sheath of the follicle, while the surrounding portion will become more elevated. The ducts of the sweat glands have the same relation to the epidermis and may act in the same way. It should be stated, however, that some authors do not accept this explanation, but believe that the centre of the vesicle is held down by a resistant portion of tissue from some other cause. According to Curschmann, Auspitz and Basch teach that the periphery of the vesicle swells more rapidly and thus becomes more voluminous than its centre.

When the vesicle has advanced to the pustular stage and the pock is fully developed, the umbilication disappears. This results from accumulation of the pus corpuscles, which, by maceration and tension, causes the fibre of tissue holding down the centre of the pustule to give way. When desiccation commences it is not unusual to find that many of the pustules begin to dry in their centre, and thus assume again an umbilicated appearance; but the umbilication previously described is something very different, both in its cause and appearance.

In unmodified smallpox, sometimes also in varioloid, both the papillæ and connective tissue beneath the pustules become involved in the inflammatory process, and, through the accumulation of pus corpuscles in the papillæ, the bloodvessels are compressed, producing necrosis of the upper layers of the true skin. The extent of this necrotic action determines the size and shape of the cicatrices; for wherever fibrous connective tissue is destroyed its place is supplied by cicatricial growth. Permanent scars may therefore be expected to follow the eruptive process.

The vesicles in hemorrhagic variola differ from the ordinary vesicles in that they contain blood instead of lymph and pus. In the milder cases of this form of the disease there may be only a slight admixture of blood with the elements usually found; in the severer cases not only do the vesicles literally fill with blood, but there is hemorrhagic infiltration in all the layers of the cutis and even in the subjacent areolar tissue. This latter condition is often very extensive, covering almost the entire surface of the body. In such cases death usually occurs before there is time for the development of vesicles. Wagner's investigation shows that the hemorrhagic extravasation is not the result of rupture of the bloodvessels, but is due to transudation of the altered blood through the relaxed and weakened vascular walls. Certainly no anatomical changes sufficient to account for this condition have yet been found in the walls of the vascular system.

The *mucous membranes* are not exempt from the eruptive process. The eruption on this membrane, however, rarely observes the same course as on the cutaneous surface. Instead of running through the distinct stages of papule, vesicle, and pustule, it is apt to assume the form of diffuse purulent infiltration of the layers of the epithelium, and may even become diphtheritic in character. The extent and intensity of the involvement of the mucous membrane usually bear a very direct relation to the eruption on the skin.

That part of the mucous surface which comes in immediate contact with the air is more apt to be attacked. Indeed, the mucous lining of the nose and mouth seldom escapes. The tongue, posterior nares, and pharynx are often severely attacked, even to the extent of interfering with deglutition. The eruption may occur in the larynx, trachea, and bronchial tubes, even below the bifurcation, giving rise to various grades of catarrhal inflammation. Catarrhal pneumonia occurs not infrequently.

The eruption has been found in the upper part of the œsophagus, but it is doubtful whether it ever extends to the stomach and intestines. It has, however, been seen at the lower end of the rectum close to the anus. The vulva and outer portion of the vagina are often severely attacked, and I think there is good reason to believe that the cavity of the uterus is not infrequently involved. The eruption is found at the orifice of the urethra, but the urethra and urinary bladder seem to be exempt.

The Viscera.—There are no pathological changes found in any internal organ that can be regarded as peculiar to smallpox. The liver, kidneys, and spleen have been found swollen and engorged with blood, and occasionally in a state of fatty degeneration. When the latter condition exists there is also apt to be degeneration of the walls of the heart. In the severer forms of hemorrhagic variola, where death occurs early, the heart, according to Ponfick, is contracted, firm, and of a brownish red color. In this class of cases the spleen also is small, dense, and very dark. Besides these changes hemorrhages are found in the viscera, the cavities of serous membranes, the loose connective tissue of the mediastinum, and in various other parts of the body.

The *brain* and *spinal cord* have been found congested and œdematous. Changes not well defined sometimes occur in the nervous system, giving rise to aphasia and certain forms of paralysis. Hemorrhages into the sheaths of nerves have been seen by Zülzer.

Abscesses and purulent collections in various serous cavities, as the result of septicæmia, not infrequently occur. I have several times seen large collections of pus in the pleural cavity, and also in the larger joints, especially the elbow joint.

The *eyes* are often severely affected. Conjunctivitis and œdema of the lids are common. The cornea is frequently attacked by ulcerative action, resulting often in perforation and protrusion of the iris. Suppuration of the globe sometimes follows.

SYMPTOMS.—*Incubation.*—The period that intervenes between the reception of the variolous contagium into the system and the earliest manifestation of symptoms is known as the "period of incubation." The duration of this period generally does not vary very greatly. In the majority of cases in which I have had opportunities of observing it carefully I have found it to be from ten to twelve days. It is seldom less than eight or more than fourteen days. The period can only be determined accurately when an individual is exposed to the contagium but once and for a short time. Where the exposure is frequent or extends over a long period it is not easy to determine the exact time when the contagium enters the system. When the disease prevails epidemically it is not impossible for an unknown exposure to precede the one of which the individual has knowledge, and in such case the period of incubation would appear to be unusually short. These facts may explain many cases in which this stage is believed to be either unusually long or short. When, however, infection takes place by inoculation, constitutional symptoms usually manifest themselves on the latter part of the seventh or beginning of the eighth day.

After the contagium is received into the system certain unknown processes are doubtless set up, although rarely indeed are any symptoms observed during the incubation period. Some authors describe as occasionally present such symptoms as languor, gastric disturbance, pain in the head and back, and a peculiar pallor of the face, but I have never met with any of these except toward the close of this stage. Usually the individual appears to enjoy perfect health until the invasive symptoms appear.

Initial Stage.—After slight malaise, of short duration, the symptoms of smallpox appear suddenly, and often with considerable violence. The earliest symptom is usually a distinct chill or repeated rigors; high fever follows immediately, and continues unabated until the peculiar cutaneous lesions appear. This comprises a period of from two to four days, and is designated the *stage of invasion*, or *initial stage*, of smallpox.

The chill which usually marks the beginning of the initial stage is sometimes severe, though more frequently it assumes the character of repeated rigors. While, as a rule, the latter are well pronounced, yet occasionally they are so mild as scarcely to attract attention. Synchronously with the chill or immediately following it fever appears. The temperature on the first day often rises to 103° or 104° F., and on the second and third days, with perhaps the exception of slight morning remissions, it rises still higher, frequently reaching 105°, and in some cases even 107° F. The elevation of the temperature is usually sudden; in but few diseases does it rise so quickly from the normal to a high degree. Even in varioloid the early symptoms are not infrequently equally severe, although occasionally they are so mild as to escape attention, so that the first symptom noticed is the skin lesion. But the eruption of unmodified smallpox never appears without being preceded by a well marked invasive stage.

While the fever continues the skin, of course, is hot and sometimes dry, though more frequently covered by a moderate perspiration. The pulse is full, tense, and rapid; its rapidity generally corresponds with the temperature curve. In adults it may vary between 100 and 130, while in children it not infrequently reaches 160. The respirations are almost always increased in frequency, especially when the temperature is excessively high. Prostration is often extreme, being out of all proportion to the length of the illness. Strong and robust patients are frequently unable to stand without support, and when in the upright position soon become pale, languid, and liable to be attacked by vertigo or syncope.

There is also thirst, the lips and tongue are parched and dry, and loss of appetite is manifest. Constipation is common. The tongue is usually coated with a thick yellowish covering, and the breath is heavy and offensive. According to some authors, the odor from the body of a patient at this stage of the disease is so peculiar and distinctive as to make it possible for the diagnosis of smallpox to be made by this symptom alone. I have heard of many curious instances of this kind, but I must confess that my olfactories have never acquired this degree of acuteness.

Irritability of the stomach is a very frequent symptom at this stage. It is often very obstinate, continuing for two or three days or until the eruption appears, and is apt to be accompanied by marked tenderness of the epigastrium. The irritability usually ceases when the eruption appears, but if it continues longer the case should be viewed with some solicitude. In hemorrhagic smallpox especially this symptom, together with epigastric pain, is not infrequently very prominent and distressing. Certain nervous symptoms are usually present. The most prominent is headache, which is scarcely ever entirely absent. Delirium is often seen, especially when the temperature is high. It may be mild in character, the patient simply talking incoherently, or so violent that forcible restraint is necessary. The latter form is usually attended with great restlessness and insomnia. Coma is rare, although it may be met with in children. Convulsions are very common among children—more so, perhaps, in this disease than in any other of the exanthemata. Pain in the back is a symptom so commonly observed that it is believed to be of special diagnostic value. It is not so constant as some other symptoms, yet it occurs in more than half of the cases. Like headache, it begins at the onset of the disease and continues until the eruption has made its appearance. The lumbar and sacral regions are the parts to which the pain is usually referred, although it may extend to the dorsal region. As a rule, it is more severe in unmodified smallpox than in varioloid, yet this rule is subject to many exceptions. In hemorrhagic cases the pain is often excruciating.

Pain in the back is perhaps more constantly seen among female than male patients, owing to the fact that the menstrual function is very liable to be excited by the initial process of smallpox, causing the menses to appear out of their regular period. Pregnant females also are exceedingly liable to suffer from premature delivery or abortion. The pain in the back, therefore, resulting from these causes tends to give greater prominence to this symptom of smallpox in females.

The urine is usually more or less diminished according to the degree of fever. The solid constituents are not out of their normal proportion, except the chlorides, which are considerably diminished. In severe cases, especially those about to assume the hemorrhagic type, albuminuria may be present. A high grade of fever might be responsible for a small quantity of albumin, but if it be present in great abundance, a malignant type of the disease should be suspected. Before giving an unfavorable prognosis, however, care should be taken to see that the albumin is not the result of some chronic disease of the kidneys.

The spleen, according to Curschmann, whose attention has been especially directed to it in a large number of patients, is not rarely enlarged. He says he has never been able to detect any enlargement of this organ in the initial stage of varioloid, but has found this condition present, and often to a marked degree, in unmodified smallpox. In many severe and grave cases, however, the splenic tumor was absent. Therefore no great diagnostic value can as yet be attached to this symptom.

A peculiar prodromal rash often makes its appearance during this stage. When it occurs it is usually seen on the second day of the invasive fever, and continues not longer than forty-eight hours or until the beginning of the true eruption. The frequency of this rash appears to vary in different epidemics. During the widespread and malignant epidemic of 1871–72 it was very common. Some authors describe it as presenting an erythematous or scarlatiniform appearance, but according to my observation it more nearly resembles the rash of measles. So close, indeed, is the resemblance that the first time I met with it I fell into the error of supposing the case to be one in which measles and smallpox coexisted. The name generally given to the rash—*roseola variolosa*—conveys a very good idea of its appearance.

This peculiar exanthem occurs quite as often in varioloid as in variola. In the absence of any exact data I venture the assertion that I have met with it more frequently in the former. I am able to recall at this moment two cases of variolous disease in which it was the only eruption that occurred at all. In one of these, it is true, about half a dozen small papules appeared as the initial rash faded away, but they disappeared in two or three days without becoming in the slightest degree vesicular. These belonged to the class of cases commonly designated *variola sine exanthemata*, the most benignant form of the disease that occurs, as well as the rarest. That such cases are encountered occasionally is evident from the writings of all authors, both ancient and modern. Perhaps in every epidemic patients are seen who give a history of exposure to the contagium of variola, and after the usual incubation period are suddenly seized with repeated rigors, followed by headache, fever, irritable stomach, prostration, and pain in the back; which symptoms continue three or four days, and then subside without any cutaneous manifestations, except perhaps the rash just described. It is difficult to explain such cases on any other supposition than that the disease was smallpox without the eruption.

While the initial stage may present the most varying phases, some symptoms may be entirely absent and others appear with great severity, yet there are usually no indications, thus far, to justify the certain expectation that the case will be mild or severe, modified or unmodified; this can only be clearly determined when the eruption has made its appearance, which is not until the invasive stage has passed. The duration of this stage is commonly forty-eight to seventy-two hours; it is rarely less, but it may be somewhat prolonged. There is, however, no decided remission in the fever until the second or third, and sometimes not until the fourth, day of the eruption.

Stage of Eruption.—By observing carefully the early stage of the disease it will be found that the true eruption makes its appearance with remarkable regularity on the third day of the illness, counting the day on which the initial chill or rigors occurred as the first. The eruption almost always appears first on the forehead and temples near the edge of the hair, and on the wrists. Not infrequently it may be seen first on the upper lip or near the mouth. It rapidly spreads to the scalp, face, neck, ears, forearms, and hands, always showing a decided preference for the cutaneous surface habitually exposed to the atmosphere. In the course of twenty-four hours, sometimes somewhat earlier, it extends to the body and lower extremities. Not simultaneously does it appear on these parts, but first on the back, arms, and breast, then on the legs and feet. Nor does the entire eruption make its appearance all at once on any one part, but it continues to multiply for two or three days before its definite limit is reached. A careful study of the eruption s[illegible] that the lesions are exceedingly apt to locate themselves ound the hair follicles and orifices of the glands of the skin. Another otable feature of the lesions is that they show a remarkable predilection all irritated or abraded surfaces, and hence collect in dense clusters ound an ulcer or any localized inflammation of the skin. Even the dness produced by a sinapism predisposes that part to an intensely nfluent form of the eruption. But while the lesions may thus be creased on certain areas, they do not seem to be thereby diminished other parts of the body.

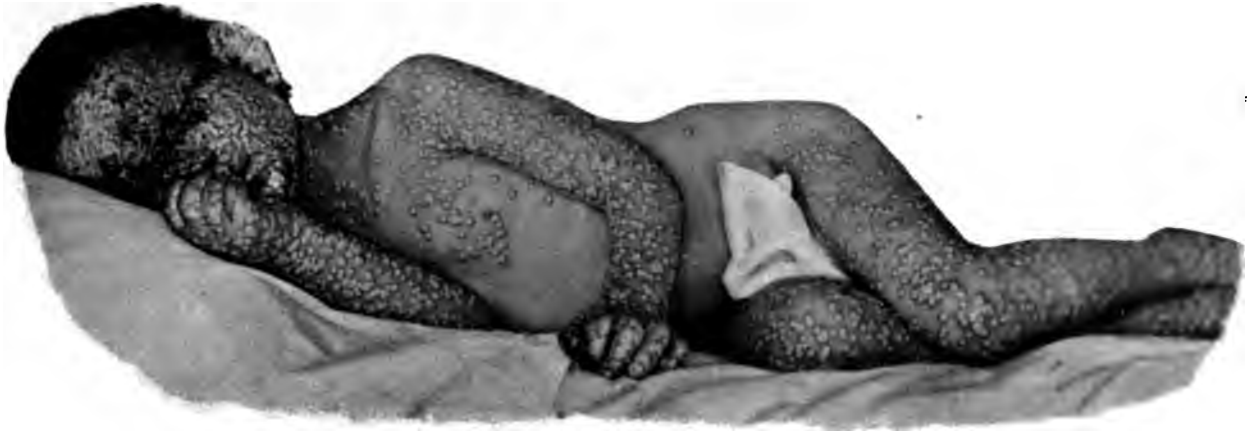
As the outbreak of the eruption is gradual, so also is its development. It usually appears in the form of minute red points, some of hich may be so small as to be scarcely visible, and others as large as mustard seed. These gradually increase in size and number, becoming more and more prominent, so that in twenty four hours they assume form of elevated papules, characteristically indurated, and convey to touch a sensation similar to what would be expected if grains of ot were buried in the skin. The papules at first are always discrete, but they may rapidly increase in number and become confluent, even before the vesicular stage is reached. At first the small red spots give rise to no subjective symptoms, but as they advance to the papular stage there is a slight pricking or painful sensation, and this increases as the lesions become more prominent.

On the third day of the eruption, or fifth day of the disease, very many of the lesions which made their appearance first will be found to contain a little clear serum. By the fourth or fifth day all the lesions are transformed into vesicles with cloudy and milky contents (Fig. 46). These continue to enlarge, attaining their maximum size about the seventh or eighth day. As soon as the vesicles form there can be seen in very many of them a central depression, which deepens as they enlarge, giving them the peculiar umbilicated appearance which has been described in a previous section. Umbilication of the vesicles is a very important diagnostic symptom in variola, since the vesicular eruption of no other disease presents exactly the same appearance.

A close examination of the vesicles shows that their interior is divided into many partitions or cells. This is evident from the fact that if a simple puncture be made into the epidermic covering of a vesicle only a small part of its contents will escape through the opening, while the principal part remains undisturbed.

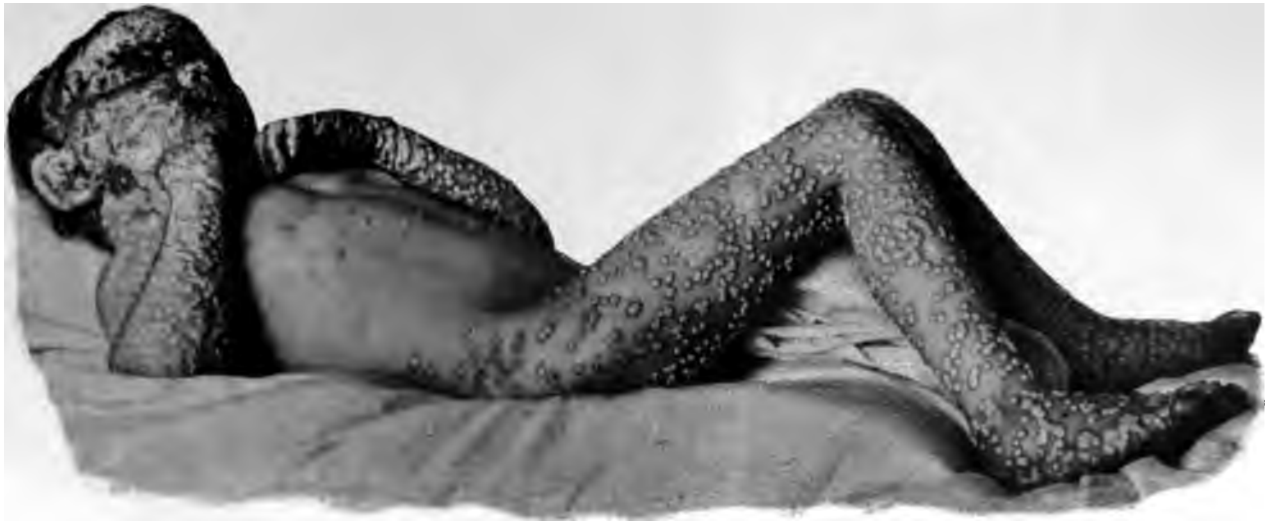
Stage of Suppuration.—The contents of the vesicles gradually grow more and more turbid by the constant accumulation of pus corpuscles until it becomes distinctly purulent. This condition is usually reached in unmodified smallpox about the sixth day of the eruption, and marks the beginning of the stage of suppuration. The pustules now in good part become large and globular, losing to a great extent their umbilicated character. The efflorescence or areola which at first surrounded them becomes broader and more intense, causing the skin in their immediate vicinity to present an inflamed and tumefied appearance. On parts of the body where the pustules are thickly set, particularly on the face and head, the redness and tumefaction are extreme, often distorting the features to such an extent as to make the patient unrecognizable. The eyelids are frequently so œdematous that they cannot be opened, and

PLATE VI.



Variola on the Seventh Day of Eruption. Confluent on Face and Semi-confluent on Extremities.

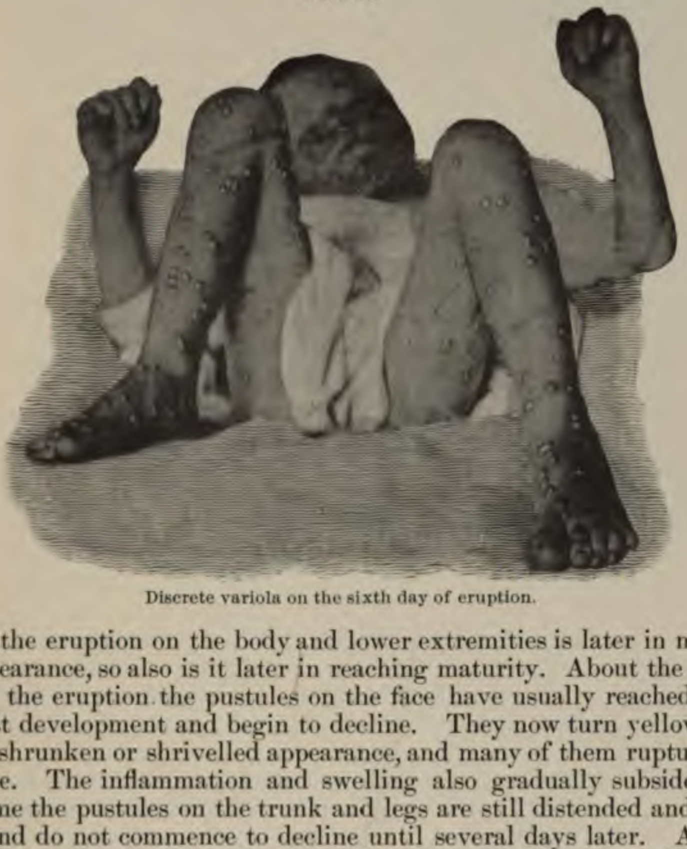
PLATE VII.



Variola on the Eighth Day of Eruption. Confluent on Face and Semi-confluent on Extremities.

mucus or puriform secretions collect at their margins; the lips, nose, and ears are greatly swollen; and the scalp is often so swollen and painful that pressure from the pillow is scarcely endurable.

FIG. 46.



Discrete variola on the sixth day of eruption.

As the eruption on the body and lower extremities is later in making its appearance, so also is it later in reaching maturity. About the eighth day of the eruption the pustules on the face have usually reached their greatest development and begin to decline. They now turn yellow, present a shrunken or shrivelled appearance, and many of them rupture and collapse. The inflammation and swelling also gradually subside. At this time the pustules on the trunk and legs are still distended and globular, and do not commence to decline until several days later. At this stage of the disease a peculiar sickening odor emanates from the body which in severe cases is extremely offensive.

The eruption on the trunk is almost always much less abundant than on other parts of the body. Not infrequently the hypogastrium is quite free from pustules, even when they may be seen on the face and hands in a confluent form. (See Plates VI. and VII.) The pustules on the trunk also seem to set more superficially on the skin than those on surfaces habitually exposed to the atmosphere; hence they are not accompanied by the same amount of painful tumefaction nor as great ulcerative destruction of the cutis. During the period of maturation the fingers and toes are often excessively painful. This condition has been not inaptly compared to a paronychia on each finger. The cause of the suffering is not difficult to explain. As the pustules develop into the callous covering of these parts they are prevented from projecting outward by the hard and unyielding epidermis, and hence considerable pressure is made on the network of nerves which lie between the pus-bone. On the palms of the hands and soles of the feet the les never project as on other parts of the cutaneous surface.

ultaneously with the appearance of the eruption upon the external e of the body certain portions of the mucous membrane also e involved. If an examination of the mouth and fauces be made very beginning of the eruptive stage, small yet distinct red spots be seen on the roof of the mouth, buccal surfaces, and the anterior nes of the palate. Almost always is the involvement limited to those ts of the mucous membrane which are near the external orifices of mucous tract, such as the mouth, nose, and pharynx.

The extent of the lesions on the mucous membrane bears a very direct tion to the intensity of the eruption upon the skin. In severe cases, he disease advances toward the stage of suppuration, the eruptive ocess extends from the to the fauces, pharynx, and ometimes to the larynx, using so much inflammation, swelling, or œdema as to m ition difficult or impossible, or causing hoarseness or complete aph nd not infrequently acute œdema of the glottis, even to the extent ously impeding respiration. The lesions may extend into the trachea, but rarely below the bifurcation. They often attack the tongue severely, and occasionally set up an intense form of glossitis, causing the organ to swell so enormously as to prevent its retention wholly within the mouth. So peculiar is this condition of the tongue that the earlier authors speak of it as *glossitis variolosa.*

Much annoyance is often experienced from the presence of the eruption in the nasal cavities. The mucous membrane at first is inflamed and swollen, and later the nares are obstructed by the formation of scabs, rendering breathing through the nose difficult and sometimes impossible. The eruption may be seen on the vulva, sometimes in the vagina, and occasionally in the lower part of the rectum; but on these parts it is not apt to be very abundant. Rarely is the urethra attacked, except at the meatus.

The eruption on the mucous membrane presents a very different appearance from that on the skin. It does not conform to the stages of papule, vesicle, and pustule. Taking, for example, the mouth, the lesions at first appear as minute red spots, much deeper in color than the mucous membrane itself, and, as the eruption on the skin becomes vesicular or pustular, they assume a whitish or grayish appearance, with but little if any elevation above the surface, rather than the form of distinct vesicles. There is perhaps an effort on the part of nature toward the formation of vesicles, but the thin and delicate epithelium which should serve as their covering is at once destroyed by the macerating influence of the mucous secretions. In severe cases the mucous membrane is usually so denuded of its epithelium, swollen, and painful that mastication is impossible, and the patient is therefore forced to subsist entirely on a liquid diet.

As already indicated, the febrile symptoms are well marked during the invasive stage, the temperature often jumping to 106° F. or even higher immediately after the initial chill. It is commonly believed that the temperature falls as soon as the eruption appears, but I have found that the fever continues high until the third or fourth day of the eruption, when there usually occurs either well marked remission or complete apyrexia. In very mild cases the fever of course abates or subsides earlier. The fall of temperature at this stage, even in severe cases, is not infrequently very rapid—so rapid, indeed, as to drop from a high degree to normal, or even subnormal, in the course of twelve to eighteen hours. The difference between the morning and evening temperature is not great, although the latter, as a rule, is slightly higher.

When the temperature falls there is usually amelioration of all the symptoms. The pulse becomes almost normal; the respirations are easier; the pain in the back, headache, and irritability of the stomach all disappear, except in critical cases; the delirium ceases, and comparative comfort ensues, enabling the patient to rest and enjoy refreshing sleep. Even the appetite returns, and the transformation is so great that the patient is apt to imagine the critical period of the disease has passed. The subsidence of the symptoms, however, is never so absolute in *variola vera* as in varioloid. In mild cases of the latter all subjective symptoms often disappear, not to return again, and convalescence dates from this time; but in the former the chief danger is yet to be encountered.

At or shortly after the commencement of the stage of suppuration the temperature again begins to rise, and continues high until the decline of the eruption, or longer if complications occur. This rise constitutes the secondary or suppurative fever of smallpox. When the disease is not very severe the temperature may not rise above 102° or 103° F., but in well marked confluent cases it frequently reaches 104°, rarely exceeding that point unless the case be very critical, when it may rise to 105° or 106°, and I have known it to reach even 107° F. The variation between the morning and evening temperature now is greater than at any previous stage; a difference of 2° F. is not uncommon. As this is truly a suppurative fever, the rise of temperature bears a very direct relation to the cutaneous involvement. The pulse usually runs parallel with the temperature curve, varying between 100 and 140 beats in a minute. With the increase of fever other symptoms appear. The pain and suffering are now much greater than before; heat and burning sensations are complained of; there is great restlessness and sleeplessness; headache and delirium may return; and the patient's life is often in great jeopardy.

Disturbance of the cerebral functions is not seldom a very prominent feature during the stage of suppuration. The high temperature, together with the intense congestion and tumefaction of the face and head, doubtless produce hyperæmia of the brain, and from this condition, with some peculiarity of temperament, the various forms of delirium arise. Sometimes the delirium is mild; the patient simply talks incoherently in a low, muttering tone; at other times he may be very restless and uneasy, constantly trying to get out of bed and to escape. Then, again, the delirium may assume such an intense character that unless forcibly restrained the patient is liable to seriously injure either himself or his attendant. A strong tendency to self-destruction is often manifested, and warrants the utmost precautions for his safety, even the use of the strait jacket if the man be large and powerful. It is not difficult to see by the countenance of the patient that he is moved by an evil impulse, for his eyes are wild and his expression fierce. Hence the name *delirium ferox* was given to this form of cerebral disturbance by the earlier authors.

In an advanced period of the stage of suppuration, especially in ere and critical cases, the nervous disturbances are not unlike those iliar to surgeons as the result of extensive burns and scalds. Low, ttering delirium, general tremors, subsultus tendinum, a rapid and mulous pulse, a dark red, dry tongue, involuntary evacuations, labor- us breathing, and a collapsed expression of the face are not infrequently the precursors of a fatal termination.

Stage of Desiccation.—The pustules having attained their greatest development, maturation being completed, begin to dry and shrink. This condition marks the beginning of the last stage of the eruption, that of desiccation. As the lesions make their appearance on the face and hands first, naturally desiccation commences there. This stage usually begins about the eleventh or twelfth day of the eruption; in mild cases it often begins earlier, and in very grave cases later. If the case is to end in recovery, there is at this time not only improvement in the local, but also in the general, symptoms. The redness and tumefaction of the skin lessen, the eyes open, and the fever subsides, either gradually or rapidly according to the extent of involvement of the skin and mucous membrane. In favorable cases the temperature each day approaches more nearly the normal standard, and there is also a corresponding lessening of the pulse rate. If there be considerable dermatitis, the temperature falls less rapidly, or if complications arise, it continues more or less elevated according to the nature of the concurrent disease. But it must be borne in mind that the vital powers of the system have by this time been severely taxed, and while the temperature may be steadily decreasing, the patient is often in great danger from extreme exhaustion.

About the time the pustules have attained their maximum size and begin to shrink an exudation of a sticky, gluey nature appears on their surface. This, at first, is yellowish in color, and, when it has dried, forms a rough, brown coating on the pustules. It is at this period of the disease that the offensive odor previously mentioned becomes most marked, and in some cases almost unbearable, especially when the contents of the pustules discharge and decompose on the skin, or soak into the body linen and bedclothing and there undergo decomposition.

The remaining contents of the pustules now begin to dry and scabs are gradually formed. The drying frequently begins in the centre of the pustules, causing a depression or secondary umbilication. Not only does desiccation commence on the exposed portions of the body, such as the face and hands, but the scabs which form there are thicker and more firmly adherent than on the trunk and extremities. On the palms of the hands and soles of the feet the pustules dry earlier than on other parts of the extremities, and the scabs adhere much longer. This is owing to the fact that the pustules never acuminate here, as on other parts of the body, but remain bound down under pressure by the thick and, in the laboring class, horny epidermic covering, so that the scabs which form are flat and imprisoned, as it were, by this covering. Patients are frequently obliged to make use of artificial means in order to expedite the removal of these scabs.

When desiccation commences an itching sensation often takes the place of pain. This sensation is sometimes so insufferable that it is difficult for the patient to refrain from scratching. Children may destroy in this way the pustules over the entire face, leaving simply an abraded, bleeding surface. To prevent this occurrence it is often necessary to muffle their hands. There is perhaps no objection to destroying the pustules, provided the derm receives no injury; but constantly removing the scabs as fast as they form by forcible means necessarily inflicts additional injury on the derm, and the resulting scars are thereby rendered more unsightly. When fully formed and cicatrization is completed they separate and fall with variable rapidity from different parts of the body.

In regular cases of *variola vera* it usually requires, after desiccation has commenced, from three to four weeks for all the scabs to fall off. This makes the entire duration of the disease about five or six weeks. It is sometimes shorter, and often much longer. After the scabs have fallen the skin presents a red, spotted appearance and is disfigured by scars. These are always deeper on surfaces habitually exposed to the atmosphere, as the face and hands, than on other portions of the body. On some parts of the face, particularly on the nose, the destruction of the derm is often so great as to produce large radiated scars, very unsightly in appearance and persisting for a lifetime. The scars at first are red, but after many months become much paler than the normal skin. While the scabs are separating and falling, and for a short time subsequently, the greater part of the hair also falls out, especially when the eruption has been very abundant on the scalp; but it is almost always restored again. The nails may suffer in the same way, but only in extraordinarily severe cases.

If serious complications do not occur, convalescence is usually rapid, in spite of the more or less numerous furuncles which are so exceedingly common. The appetite returns, and is generally keen, sometimes even voracious. The digestive functions are active, and the patient rapidly regains strength and flesh until restoration of health is complete.

VARIETIES OF SMALLPOX.—Reference should be made to other forms and varieties of smallpox before its clinical history is complete. The course above described relates more particularly to that form of the disease in which the eruption is either discrete or semiconfluent. According to my experience, the vast majority of cases commonly met with belong to the latter variety; that is to say, the eruption is usually either partly or wholly confluent on the face, the dorsal surface of the hands, and the lower portion of the forearms, while on the trunk and extremities it is discrete, except that many of the pustules on the extremities may coalesce. Variations from this form may reach extreme limits, from a few small pustules, scarcely definite enough to verify the disease, to the most extensive eruption covering the entire cutaneous surface. Also types of the disease presenting widely divergent clinical features still remain to be considered: I refer to the petechial, purpuric, and hemorrhagic forms of smallpox.

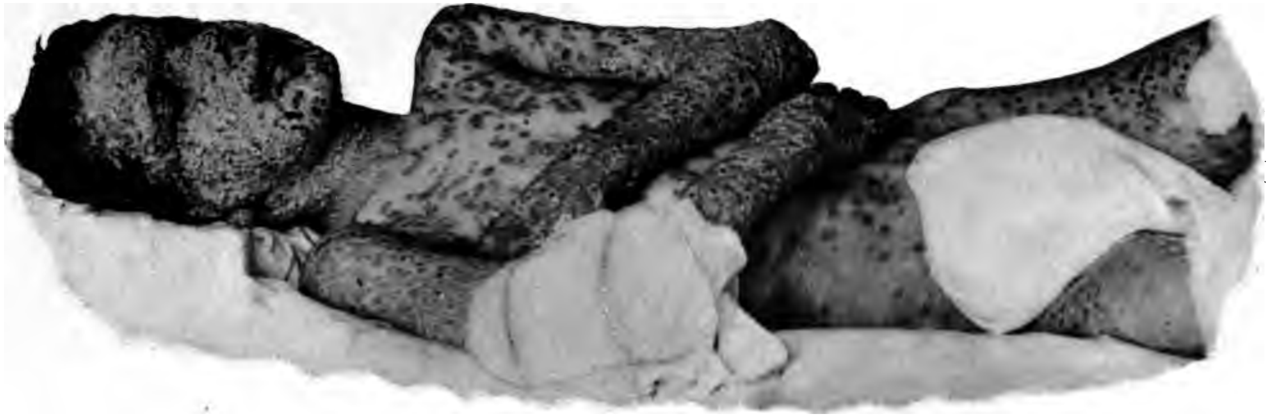
Confluent Variola.—It can hardly be said that there is any symptom during the initial stage of smallpox peculiar to the confluent form of the disease. The symptoms, however, are always severe in this variety, while in varioloid they may be either severe or mild; hence a mild g d warrant the exclusion of the confluent type. Most ent amo the early symptoms are severe headache, persistent g and vo iting, wild delirium or stupor in children, violent pain back, and igh fever. The temperature always rises rapidly, and ntly atta an extraordinary height. Its maximum height is less than 05° or 106° F., and it has even been known to reach . After he eruption has fully appeared the temperature falls ly, but rarel descends as low as in milder cases; nor does the re- ion of the ver continue as long. During the remission the tem- re is usu y not far from 101° to 102° F., and after remaining s compara vely low degree for two or three days the secondary commences. The temperature during the stage of supparation does usually rise as high as in the initial stage, yet I have known it to go siderably higher. 533) illustrates the tempera- ture curves of a s variola recently under my observation; the te er urative stage, however, was somewhat influenced retics.

The eruption in conflu ps less rapidly than in modified forms of the disease, but horter interval between the time of its appearance on the face other portions of the body. So quickly is the eruption diffused the whole body that it has been mistaken, in the papular stage, for measles. On account of the extensive involvement of the skin redness and swelling begin early. Even as early as the second day of the eruption the skin is quite red, and often it can be determined at once that the disease is going to assume the confluent form. As the eruption progresses it passes through the usual stages, though somewhat more slowly than in milder cases. The papules are thickly set: many of them coalesce, and when the vesicles develop they run together so completely as to cover almost the whole cutaneous surface. On the face and hands the septa within and between the pustules often give way and large blebs or bullæ form. Usually, however, the pustules do not acuminate or project from the surface, as in the discrete variety, but remain flat, especially on the face, and sometimes present a milky or pasty appearance. When the eruption is fully developed every feature of the patient is so changed and disfigured as to make recognition impossible even by his nearest friend (Plate VIII.).

In this form of the disease the mucous membrane of the mouth, throat, and nose is always severely affected. The epithelium of these parts frequently becomes so completely disorganized by the eruptive process that it presents the appearance of diphtheritic membrane. Swelling of the soft palate and tonsils is often so great as to cause considerable difficulty in deglutition. It is in the intensely confluent cases that *glossitis variolosa* is apt to occur. The parotid glands sometimes become acutely inflamed, perhaps by extension of the inflammation along the ducts of Steno. The pharynx and larynx are almost always attacked with great severity, and acute œdema of the glottis, interfering seriously with the respiratory act, is not an infrequent occurrence. Death undoubtedly results at times from the intense involvement of these parts.

When the contents of the pustules begin to ooze and drying commences the stench is often unbearable. The exhaustion arising from

PLATE VIII.



Confluent Variola on the Fourteenth Day of Eruption. Showing a Collapsed Condition of the Pustules and the Commencement of Desiccation.

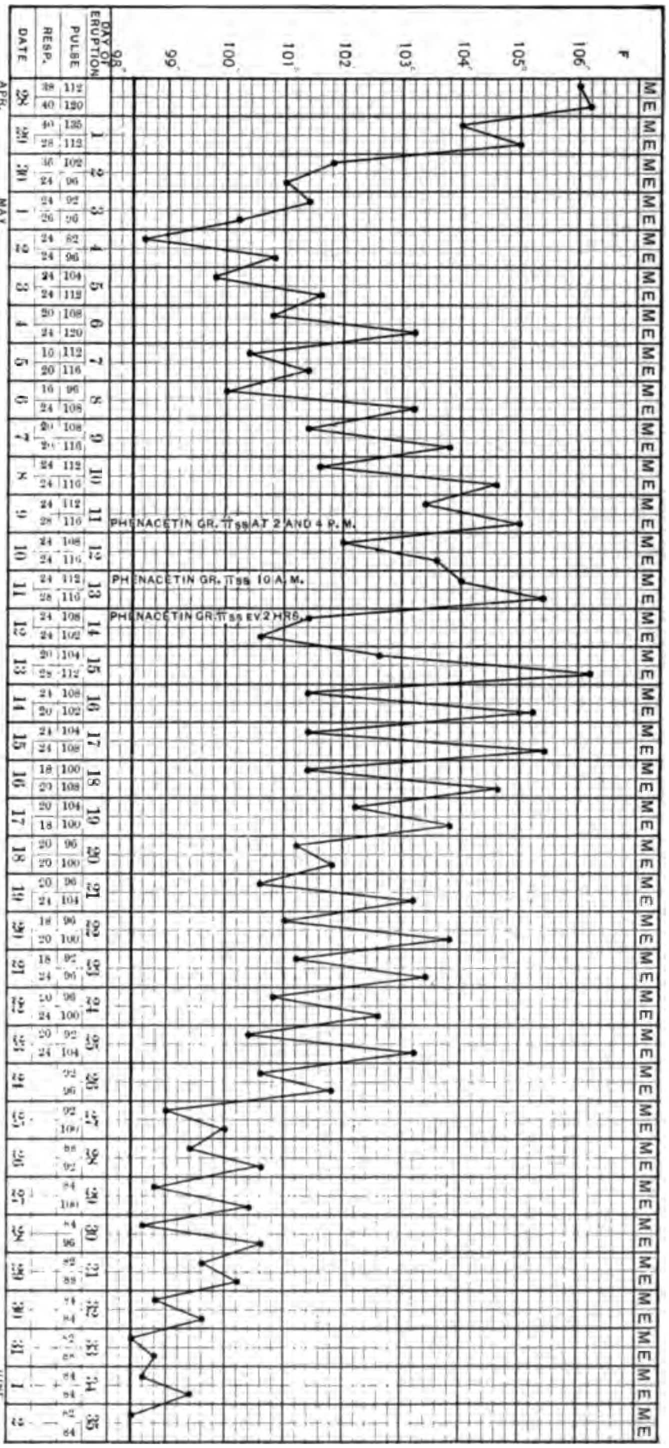


Fig. 47.

Temperature record of confluent smallpox.

irritation and extensive suppuration is, at this time, extreme, and generally constitutes the chief source of danger. At this stage, also, complications are liable to occur, such as ulcer of the cornea, purulent forms of keratitis, pneumonia, pleurisy, empyema, suppuration of the joints, and gangrene of portions of the cutaneous integument, especially of the scrotum. An uncontrollable diarrhœa frequently sets in and aids in diminishing the vital forces. The mortality from confluent variola is, of course, very great. If death does not occur from exhaustion, it is liable to result from septicæmia, pyæmia, or some one of the other complications just named.

When this form of the disease terminates in recovery it is only after a long and tedious illness and a tardy convalescence. During desiccation the inflammation and swelling of the skin and mucous membrane subside, and the patient is able to take nourishment more freely. The scabs form into large coherent masses, and some of them remain for a long time firmly adherent, especially those on the face. After they have fallen off the skin is very red and spotted, and left permanently disfigured by unsightly scars. During the period of falling of the crusts various sequelæ are liable to appear, among which furuncles are most common. Large abscesses also may form on various parts of the cutaneous surface; the cellular tissue beneath the scalp seems to be peculiarly liable to this process.

Petechial, Purpuric, and Hemorrhagic Variola.—These names are applied to the different phases presented by malignant or hemorrhagic smallpox. In certain epidemics a petechial eruption is frequently seen at the close of the initial stage of the disease or about the time the true eruption appears, or should appear if it is not delayed, and is generally the precursor of a train of symptoms indicating great malignancy. This eruption is often quickly followed by the purpuric or hemorrhagic variety, and the disease rapidly runs its course to a fatal termination. At other times petechiæ and ecchymoses appear between the papules or vesicles, and as the latter develop many of them fill with a sanguino-purulent fluid, while others fill with distinctly purulent matter; thus a great diversity is sometimes manifested in the eruption of a single case. While such cases usually result fatally, yet, if the dyscrasia is not too great, they may terminate in recovery. There is no doubt that in all cases of hemorrhagic variola the blood is greatly altered, and even in most cases so completely devitalized as to be incapable of maintaining the vital functions. Therefore recovery from this form of the disease, especially when well marked, is quite exceptional.

The causes leading to the hemorrhagic type of smallpox are, as yet, unknown. There is no doubt that such cases result from the ordinary variolous infection, and that the infection derived from them may in turn give to the disease its typical aspect. It is known, however, that this type of the disease varies in frequency in different epidemics.

Variola purpurica is the gravest and most malignant form of the hemorrhagic type. The initial stage in such cases does not differ very greatly from that of ordinary variola. There is nothing peculiar about the rigor, fever, and headache; the pain in the back, however, is intense and the prostration is generally excessive. Toward the end of the initial stage a diffuse efflorescence appears on various parts of the trunk and extremities, while the face remains for a time exempt. The rash at first is scarlatinoid in appearance, and disappears partially under pressure; later it becomes more intense; petechiæ, vibices, and ecchymoses appear, especially on the chest, the axillæ, the lower portion of the abdomen, the groins, the legs; and the dark red or purplish discoloration now present does not fade in the least by pressure. The discoloration rapidly extends to the face, which also becomes swollen and puffy. The conjunctivæ are injected; the eyes become bloodshot and surrounded by dark rings, owing to hemorrhage into the cellular tissue of the lids. Frequently the hemorrhage under the conjunctiva covering the sclerotica is so great as to cause the conjunctiva to project beyond the lids, like a sac filled with blood, and prevent the eyes from closing, while the cornea remains unaffected and looks as if it were deeply sunk into the globe of the eye. This condition, together with the dark discoloration of the face and the tumefied features, gives to the patient a peculiarly hideous appearance. A close examination of the body often reveals in certain localities, particularly the axillæ and groins, small and indistinct vesicles thickly set and filled with bloody serum. These vesicles never develop to any extent, but remain perfectly flat, and are of a blackish or leaden gray hue. As the disease progresses the dark discoloration of the skin deepens on all parts of the body, until at last it is sometimes difficult to say, judging from the color alone, that the patient is not a native of Africa. Hence this form of the disease has long been known by the name of *variolæ nigræ*. The eruptive process does not always afford unequivocal evidence of smallpox, and the disease is therefore sometimes mistaken for some other malignant affection, such as black measles and the like.

In this, as in other severe types of variola, the pharynx and upper part of the air passage usually suffer. There is apt to be more or less cough, with bloody sputum. The tongue is large and red, and the breath often horribly fetid. Indeed, the odor from the body also is extremely loathesome. There is persistent nausea and vomiting, and almost always severe pain or distress in the precordial region. The temperature is seldom very high, except in the invasive stage, but the pulse is rapid and feeble. Hemorrhages are quite certain to occur from the nose, bronchial mucous membrane, kidneys, rectum, and uterus. Women almost always suffer from metrorrhagia and, if pregnancy exists, abortion. According to my experience, this type of smallpox occurs as commonly among young and robust persons as among those infirm or debilitated. Intemperate persons and drunkards, as well as lying-in women, seem peculiarly predisposed to this terrible form of the disease.

One of the most extraordinary features about this fatal malady is that the mental condition of the patient often remains undisturbed until almost the last moment of life. There may be delirium or stupor, but usually the victim faces death with his mind clear and intellect unimpaired. I remember on one occasion, as I stood by the bedside of a most malignant case of purpuric variola, not thinking that the patient was conscious, of remarking to the resident physician that there was no ground for hope in this case. At once the patient sat up in bed and, quired, "Doctor, do you mean to say I can't get well?" than twenty-four hours the patient was a corpse.

course of this type of smallpox is very rapid. Death not intly takes place in consequence of the greatly altered state of the before any clear and well pronounced symptoms of the disease n. More commonly the eruption may be seen in confluent form on parts of the body, but it never makes much progress. Death y results from the fourth to the sixth day. I have never known a marked case to recover.

e hemorrhagic type of smallpox may assume still another form: I r to the form which Curschmann designates *variola hæmorrhagica pusa*. In this variety, as soon as the vesicles appear, instead of filling serum they fill with a sanguinolent fluid. In some cases the vesifirst appear, and imme[illegible] contents become mixed with od; in still other cases this ch[illegible] does not occur until the eruption as reached the pustular stage. [illegible] hemorrhagic condition of the pusules may be limited to certain localities or it may extend over the entire body. Petechiæ and purpuric spots, as already described, may be associated with this form of eruption. The hemorrhagic pustules usually begin on the legs, although they may appear first elsewhere. An early examination in a case about to assume this condition shows that here and there a pustule presents a blue centre; by degrees others take on the same appearance, and the color gradually deepens, until at last, in severe cases, the pustules on all parts of the body become distinctly hemorrhagic. At the same time, livid spots may be seen on the mucous membrane of the mouth and fauces. The gums are spongy and bleed readily. Hemorrhages occur from the nose and various internal organs, as in *purpura variolosa*. It is seldom, indeed, that hæmaturia is absent or that metrorrhagia fails to occur in females.

This form of hemorrhagic smallpox is more protracted in its course than *purpura variolosa*, but almost as certain to end fatally. My own experience leads me to say that recovery from this type of the disease is extremely rare; even the so-called milder cases, or those in which the symptoms are least pronounced, almost always terminate fatally. I have seen recovery in but few cases, and only among those in which the hemorrhagic condition of the pustules was not only limited to a comparatively small number of these lesions, but appeared at a relatively late period of the disease, and in which the hemorrhage from the nose and internal organs was not excessive nor long continued. I have never known recovery to result in a case in which all or nearly all of the vesicles assumed the hemorrhagic character at an early stage, and in which there were well marked epistaxis, hematuria, conjunctival hemorrhage, and bloody stools, together with the usual concomitant symptoms, such as a rapid and feeble pulse and the peculiar livid, purplish, or indigo color of the skin.

VARIOLOID.

Varioloid is not a disease which simply resembles variola, as the name would imply, but is truly smallpox in a modified form. This is evident from the fact that the infection arising from this milder form of the disease gives rise to variola vera in unprotected persons. Since the introduction of vaccination varioloid has become much more frequent than in former times. It is well known that the immunity conferred by vaccination, although complete at first, becomes through lapse of time more or less impaired in the vast majority of individuals. The protective influence from this measure frequently diminishes very gradually for a variable length of time, and eventually may disappear entirely. Hence persons previously vaccinated are liable to suffer from various grades of smallpox according to the degree of protection remaining. In every epidemic of the disease cases are seen not only so mild as to be scarcely recognizable, but also so severe that when they have finished their entire course the physician is in doubt as to whether the attack should be called variola or varioloid. It has been my rule to classify as variola all unvaccinated cases, all malignant cases, and all vaccinated cases in which the eruption pursues its regular course and is attended by secondary or suppurative fever, while I classify as varioloid all vaccinated cases in which the eruption is markedly abridged in its course, and in which there is but little if any secondary rise of temperature. Of course it is well known that in some unprotected persons there is naturally but slight susceptibility to the infection, and that the disease among this class is mild and of short duration; but such cases should be regarded simply as mild forms of variola vera. Besides vaccination, the only circumstance which determines the occurrence of varioloid is a previous attack of variola.

Varioloid cannot always be distinguished in the initial stage from *variola vera*, since the train of symptoms may be the same in each and equally severe. Occasionally, however, in varioloid the eruption appears after an exceedingly mild initial stage; this almost never occurs in unmodified smallpox. The length of the initial stage is also variable. While the duration of this stage in variola is quite uniformly three days, in varioloid it may be as short as twenty-four to forty-eight hours, or as long as four or five days. At the commencement of the invasive stage the temperature at once becomes more or less elevated: if it should rise very high, it usually drops suddenly at the outbreak of the eruption to the normal degree or even below, and does not again rise to any considerable extent unless complications occur. The initial exanthem, which has already been described as frequently appearing at this stage of smallpox, is, I believe, much oftener met with in varioloid than in *variola vera*. Indeed, this prodromous rash, not unlike measles in appearance, is so frequently followed by an exceedingly sparse variolous eruption that it might almost be regarded when present as the forerunner of varioloid. But if the rash should be petechial or purpuric in character, it is an indication that the attack will be severe.

There is nothing peculiar about the eruption of varioloid except that it is milder in its course and of shorter duration than that of variola. It almost always appears on the face, and rapidly spreads to other parts of the body, although at times it makes its appearance on the trunk and extremities quite as early as on the face. The lesions do not develop quite as regularly as in unmodified smallpox, it being not unusual to find some pustules larger and farther advanced than others.

extent of the eruption and the duration of its course are also ble. It may be limited to a very few lesions on the face and s, or it may assume a semiconfluent form on these parts, and also le other parts of the body to a considerable extent. In the milder the lesions do not pass through all the stages, but become abor- t an early period; in the severe forms the eruption passes through various stages of papule, vesicle, and pustule, and is quite as pro- nced as in unmodified smallpox. Between these two extremes the ption may assume every possible phase. It may appear in the con- nt or semiconfluent form, as just stated, but, instead of the inflam- tory action extending to the deeper layers of the skin, as in *variola* *a*, it is limited to the upper layers; hence the course of the eruption horter, desiccation occurs earlier, the scabs fall off more rapidly, and scars are not so deep. This variety of smallpox was called by ear- authors "confluent superficial." More frequently the eruption of varioloid is less copious, but runs the same mild course. The papules ery early assume the vesicular character and reach the pustular stage on the third or fourth day, completing their development from the fifth to the seventh day, when desiccation begins. The pustules dry up quickly, forming thin brownish crusts, which fall off much sooner than in the unmodified form of the disease, leaving either very superficial scars or slightly pigmented spots which entirely disappear in the course of a few months.

When the modification of the eruption is still greater, it is not unusual to find that the lesions develop into large, solid, conical papulæ, having at their apices a vesicular condition which rapidly desiccates and forms very thin crusts. After the crusts have fallen off the lesions remain tuberculated for some time, especially on the face, looking not unlike warty excrescences; to this form of the eruption the name *variola verrucosa* has been given. Another somewhat common form of the eruption is that known as *variola miliaris*. In this the majority of the vesicles are very small, not larger than millet seeds, and, without progressing any farther, turn yellow and rapidly disappear. Not rarely a few tolerably well developed pustules are found mixed with these smaller lesions. Still other varieties of the varioloid eruption have been described, and, according to the fancy of the author, designated by various terms, such as *variola siliquosa*, *v. pemphigosa*, *v. globulosa*, *v. crystallina*, etc.; but as these varieties are of no practical importance, a description of them here is deemed unnecessary.

The mucous membrane of the mouth and upper air passages is usually affected, although much less severely than in unmodified smallpox. Diseases of the eye, such as photophobia and corneal ulcer, may occur, and secondary phlegmonous processes, such as abscesses and furuncles, may follow, but these affections are also less apt to be severe.

COMPLICATIONS AND SEQUELÆ OF SMALLPOX.—The skin is more frequently the seat of complications and sequelæ than any other part of the body. Erysipelas occasionally appears when desiccation is completed and the crusts begin to fall. It more frequently attacks the face, but may appear on almost any part of the cutaneous integument. I have known it to assume a phlegmonous character on the neck and upper portion of the chest, rendering these parts as dense and unyielding to the touch as if covered with a plaster-of-Paris dressing. During desiccation gangrene of the skin, especially of the scrotum, may appear. I have met with this complication several times, and the result has always been fatal. By far the most common complications and sequelæ are furuncles and abscesses. But few patients pass through an attack of *variola vera* without suffering from numerous boils during the latter stage of the disease.

Next in frequency to the skin, the eye is most liable to suffer. During the active stage of smallpox conjunctivitis is common, and often associated with severe œdema of the lids, preventing the eyes from opening. In the stage of desiccation a small vesicle filled with clear serum often appears at the margin of the cornea. The covering of this vesicle is very thin and delicate, and almost always ruptures and disappears unnoticed, leaving a distinct ulcer covered by a little necrotic tissue of a light gray color. This condition is almost always followed by impaired vision; it frequently leads to keratitis, iritis, perforation, and sometimes suppuration of the globe, causing complete blindness.

In severe cases inflammation and swelling of the tongue occur; the larynx also is usually involved in the inflammatory action, leading often to œdema of the glottis. Perichondritis laryngea, sometimes followed by necrosis and abscess, has been met with by various observers. Bronchitis, catarrhal pneumonia, and pleuritis with purulent effusion are not infrequent complications. The mucous membrane of the nose is usually inflamed, and sometimes is the seat of ulceration.

The middle ear may suffer from inflammation, which may lead to chronic suppurative otitis, and even to caries of the bones of the ear, causing partial or complete deafness. The mastoid cells also may become filled with pus, and occasionally suppurative thrombosis of the cerebral sinuses occurs.

One or more of the joints may become swollen and painful. Sometimes perichondritis, and even ostitis, occur, followed by suppuration and destruction of the joint, and frequently by death. According to my observation, the elbow joints are most liable to suffer. Occasionally symptoms of pyæmia or septicæmia appear in the early stage of desiccation. Abscesses in the liver and lungs have been revealed by autopsies. The circulatory system rarely suffers from secondary affections. Phlebitis, however, has been met with, especially in the lower extremities, giving rise to phlegmasia dolens.

Smallpox is singularly exempt from abdominal complications. Diarrhœa not unfrequently occurs as the result of some derangement of the digestive function. While this symptom is usually controllable, yet occasionally it is so persistent as to precipitate a fatal issue in those greatly debilitated from the primary disease. The kidneys are not apt to suffer, except in malignant cases. In such cases albuminuria is present, and frequently also hæmaturia.

In the pregnant female abortion or premature delivery is very liable to occur, and this accident usually proves to be a very serious complication. As already shown, the parturient condition favors the development of the petechial or hemorrhagic form of smallpox.

Secondary affections of the nervous system are not rare in smallpox.

I do not refer to the delirium which is so common in the stage of severe cases, but to the psychical disturbances and various s of paralysis which sometimes appear during the decline of the se. Meningitis is not common, although it occasionally occurs. e oedema of the brain is perhaps more frequent. I have met with cases in which there were peculiar psychical disturbances, followed phasia: this symptom would seem to indicate the existence of mscribed encephalitis. Certain portions of the spinal cord also r at times from inflammatory action, giving rise to paralysis of the remities and bladder. In his study of such cases Westphal has nd numerous foci of inflammation in the gray and white matter of cord. According to my experience, it has always been the motor ves which were affected, and, so far as I have been able to follow the es, recovery from the paralysis eventually resulted.

DIAGNOSIS.—It is only in the initial or early period of the eruptive tage that *variola vera* is at all liable to be confounded with any other affection: in the more advanced stages this typical form of the disease is readily recognized by its peculiar manifestations. But in the modified forms of the disease, especially when the eruption is scanty or atypical, the diagnosis becomes more difficult. Great assistance may often be gained by inquiring whether the patient has ever been vaccinated, and, if so, by examining the character of the vaccine scar. Likewise, it is important to know whether the individual has previously suffered from smallpox. The diagnosis may also be greatly aided if it is known that the disease is present in the community or that there has been exposure to the contagium.

As variola is communicable during the initial stage, an early diagnosis often becomes highly important. If in a given case it be found that the patient was seized with a chill or had repeated rigors, followed by a sudden rise of temperature to an unusually high degree, and that there is present epigastric tenderness, irritability of the stomach, and severe pain in the lumbar region, variola should be strongly suspected. If, together with these symptoms, there can be obtained a history of exposure to the variolous contagium, the diagnosis becomes comparatively easy. But in many cases of variola, and especially of varioloid, the initial symptoms are so indefinite that a diagnosis is quite impossible until the characteristic eruption appears.

In making a diagnosis during the invasive stage of variola great assistance may be gained by excluding the various febrile affections more commonly met with. For example, while pneumonia usually begins with a chill, followed by high temperature, yet this disease can be excluded by the absence of physical signs. In the different forms of ephemeral fever the temperature is usually much lower. In intermittent fever there might at first be some doubt, but in less than twenty-four hours the doubt will be removed by the sudden fall of temperature. The first paroxysm of relapsing fever bears such close resemblance to the initial stage of variola as to make it difficult to differentiate until the eruptive stage of the latter disease is reached. In countries, however, where relapsing fever is rare, it need not enter into the question of diagnosis. In typhoid fever, to say nothing of the enteric symptoms, it is easy to differentiate by the very gradual and characteristic rise of temperature. Between typhus fever and smallpox in their early stages the diagnosis is sometimes very difficult. The temperature in both diseases may be equally high and the nervous symptoms very similar; but none of these symptoms are in the least abated by the appearance of the eruption in typhus, while in variola they are all greatly improved, and some disappear entirely. Likewise, in scarlet fever the temperature is high at the onset, and continues so after the rash has appeared. Not only in this respect does scarlatina differ from variola, but by the uniform diffusion of the characteristic rash, the absence of papulæ, and the presence of angina. But between purpuric variola and malignant scarlet fever the diagnosis is often very difficult, as in both affections the rash may be diffused and intensely red or purplish, the fauces are usually inflamed, and the temperature, even in variola, does not fall when the eruption appears. In such cases I would advise that the entire cutaneous surface be carefully examined: very often small hemorrhagic maculo-papules or very flat and intensely purple vesicles may be found on some parts of the body, the presence of which would be sufficient to exclude scarlet fever. It should be remembered that in this form of variola the favorite seat of the eruption is the lower abdominal region, together with the inner surfaces of the thighs near the external genitalia. Next to this locality, the hemorrhagic exanthem shows a preference for the axillary regions. Attention given to these points will often aid very greatly in the differential diagnosis between these malignant affections.

When the eruption of variola first appears it is not infrequently confounded with measles. The catarrhal symptoms, which are so prominent in measles and so rarely absent, constitute at this stage one of the most striking points of difference between these diseases. Equally important also is the degree of fever. While the temperature in the initial stage of variola suddenly rises to 104° to 106° F., in measles it is rarely higher than 102° to 104° F. In variola it falls soon after the eruption appears, while in measles it continues the same or may rise still higher. The eruption of measles frequently makes its appearance quite as early on the back as on the face, and the lesions are equally numerous on both of these localities; while in variola the eruption begins on the face and extends gradually downward. If the eruption be carefully examined, it will be found to consist of innumerable maculæ, and that the maculæ of measles are larger than the papulæ of variola; that the maculæ are set in clusters or groups, while the papulæ, even in confluent cases, are at first remarkably discrete; that the maculæ disappear or grow pale under pressure, while the color in the papulæ is more persistent; that the maculæ are soft and velvety to the touch, while the papulæ are hard and shotlike. The latter condition of the eruption in variola has always been regarded as a symptom of considerable diagnostic value—and justly so, too—yet the eruption of measles often assumes a distinctly papular character on some parts of the face, and especially on the wrists; therefore care should be taken to examine the back of the patient before making a diagnosis. But it must be admitted that the eruption of these diseases is occasionally, for a very brief time, so similar in appearance as to defy the skill of excellent diagnosticians; in such cases it is advisable to defer the diagnosis twenty-four hours, by which time the eruption in either case will rly reveal its individuality.

On account of the swelling and the vesication in facial erysipelas disease has been mistaken for variola; but a careful physical examination should be sufficient to avoid such an error. Glanders, in an stage, is said to bear some resemblance to smallpox, not only as to febrile conditions, but also as to the cutaneous lesions, which conof hard infiltrations in the skin, followed quickly by suppuration. t the lesions appear in successive crops and ulcerate rapidly; more-r, the disease is very rare and occurs only among grooms and blemen.

Rashes produced by the ingestion of certain drugs, as well as various kin diseases of a vesicular or pustular character, have been mistaken for the eruption of smallpox; but a thorough knowledge of the course and peculiar features of the variolous eruption is the physician's safeguard against such errors. Vaccination with animal virus sometimes causes an erythematous or rubeoloid rash, known as *roseola vaccinosa*, to appear from the eighth to the twelfth day of the vaccine disease. I have quite frequently known this rash to have been mistaken for the eruption of variola, especially during epidemic visitations of the disease. The distinguishing features are that it accompanies vaccinia, that it is not preceded by a very high temperature, and that it consists of maculæ rather than papulæ. If, after considering these points, the question of diagnosis cannot be clearly settled, the lapse of twenty-four hours will be sufficient to remove the uncertainty.

A certain though comparatively rare form of secondary syphilis is occasionally met with in which the eruption closely simulates that of variola. This eruption passes through the stages of papule, vesicle, and pustule. It is preceded by elevation of temperature, although the rise is not as great as in variola. To differentiate between these diseases it is necessary to inquire into the history of the case and closely observe the course of the eruption. Those who are familiar with the lesions of smallpox will usually notice at once in the syphilitic patient something about the eruption which indicates that it is not variolous, yet the distinction cannot always be clearly defined until the case has made some progress. The pustules do not develop simultaneously, as in variola, but in successive crops, and are more protracted in their course.

There is, perhaps, no disease more often confounded with smallpox than varicella. Of course this disease is very much milder in every particular than *variola vera*, and therefore liable to be mistaken only for the modified forms of the disease or varioloid. The differential diagnosis between these diseases is postponed for consideration in the article on Varicella.

PROGNOSIS.—Since the introduction of vaccination the presence or absence of a typical vaccine scar on a patient is an important factor in the question of prognosis in smallpox. Formerly, smallpox was not only more common, but uniformly far more fatal, and therefore much more dreaded, than at present. During the last century but few diseases claimed a greater number of victims than variola, but at the present time, especially in countries where vaccination is carefully and systematically practised, the proportion of deaths from this malady is not greater than $\frac{7}{10}$ per cent. of the entire mortality, and where revaccination at the proper age is also enforced this proportion is even much less. In the prevaccination period one tenth of all the children born died from smallpox; now the mortality from that disease among young children is almost *nil* where vaccination is compulsory. But after the lapse of several years the protection conferred by vaccination becomes, in most persons, either partly or wholly exhausted, so that when the variolous contagium is introduced into a community the disease is seen in every possible grade of severity, and the death rate varies accordingly.

Unmodified smallpox is an exceedingly fatal disease, the death rate varying in different epidemics from 15 to 60 per cent. The epidemic which swept over this and other countries in the years 1870 to 1872 was everywhere characterized by unusual malignancy, and the mortality among the unvaccinated cases was, in some places, as high as 64 per cent. In the absence of an epidemic influence, however, the disease is usually much less fatal. It is believed by some authors that the disease is more fatal at the beginning and during the maximum of an epidemic than when it is declining, but I am not sure that such is the case. Certain seasons of the year are also believed to exercise some influence over the mortality from the disease. It is probably true that a patient is less able to bear the depressing effects of confluent variola when the weather is excessively warm than when the temperature is cooler.

In considering the prognosis in individual cases of *variola vera* there are various circumstances to be taken into account. First of all, the age of the patient is of great importance. It is comparatively rare for an infant under one year old to survive an attack of unmodified smallpox. So also at the other extreme of life the death rate is enormous. In children from one to five years of age the disease is also very fatal, but among those from five to fifteen years old the chances of recovery are rather better than in adult life.

Sex has but little to do with the question of prognosis. Among women the mortality is somewhat increased on account of their liability to suffer from metrorrhagia or, when pregnant, from miscarriage or premature childbirth. The occurrence of either of these accidents or the presence of the parturient state strongly predisposes the patient to the hemorrhagic form of the disease. Among men intemperance adds very greatly to the danger. Drunkards or constant drinkers seem peculiarly prone to suffer from hemorrhagic smallpox. I have found almost every variety of the disease very fatal among bartenders. The powers of resistance against the exhausting influence of variola are often so diminished by chronic alcoholism that death results from a form of the disease from which a patient with a more healthy organism would recover. Mania à potu, of course, furnishes a very serious complication. Intemperate persons are apt to be badly nourished, and this condition is always unfavorable in smallpox. It need hardly be stated that the prognosis should be very guarded when variola occurs in a convalescent from some acute exhausting disease.

With respect to the danger in individual cases, it is necessary to consider not only the type of the disease, but also the separate symptoms. During the initial stage there is no reliable symptom to indicate the y the attack. Not infrequently the mildest eruption of varios preceded y a very severe febrile stage. If, however, the initial be very n l, it would be safe to prognosticate a moderate erup- Severe lu bar pains may be present in both modified and unmodinallpox, yet if they be extremely severe there would be some . to expect a hemorrhagic form of the disease. Having met with nitial exanthem (*roseola variolosa*) oftener in varioloid than in odified smallpox, I feel disposed to regard the presence of this as indicating that the true eruption will be of the modified form; t must be remembered that this peculiar exanthem sometimes pre- the eruption of variola vera.

n estimating the danger in smallpox there is usually no better guide n the quantity and character of the eruption. As the eruption in rioloid is sparse or superficial a runs a course of short duration, this rm of the disease rarely proves fatal. Discrete variola is also attended by no great danger, but confluence should always be regarded with apprehension. If the eruption be confluent on all parts of the body, the patient's condition should be looked upon as extremely perilous. In semiconfluent cases, especially when the eruption on the face is copious, the question of recovery becomes problematic. If the pustules acuminate well and are accompanied with considerable swelling, and if those on the extremities are surrounded with a crimson areola, and the patient takes nourishment freely, there is good ground for hope. If, on the other hand, the pustules on the face be flat, milky white in color, and pasty, with almost an entire absence of tumefaction, and if those on the extremities be surrounded with a dark red or livid areola, no reasonable hope of recovery can be entertained. It is also an ominous sign for evil in confluent variola to see here and there a vesicle on the face desiccating prematurely or to find some of the vesicles developing blue centres.

The chief danger in confluent variola is from exhaustion. When the entire body is covered with pustules the quantity of purulent fluid generated is enormous, and this amount of pus formation, together with the vast irritation and inflammation of the cutaneous integument, very seriously disturbs the vital powers of the patient. During the early period of maturation the patient's condition should be regarded as extremely critical if the progress of the eruption be suddenly arrested and the swelling of the face and hands subside, leaving the skin in the spaces between the pustules pale; if the pustules themselves shrink or collapse; if the pulse be rapid, dicrotic, or feeble; if the delirium and restlessness increase; or if nourishment be refused or taken very reluctantly. When confluent variola runs its regular course, death seldom occurs before the end of the first week of the eruption: the greatest danger to life is found to be during the maturative stage or the second week of the eruption.

The condition of the mucous membrane of the pharynx, larynx, and trachea should be regarded as only second in importance to the skin lesions in estimating the degree of danger in variola vera. If these parts become severely implicated by the variolous process, giving rise to such symptoms as a diphtheritic condition of the fauces, dysphagia, difficulty of respiration, or œdema of the glottis, the case should be viewed with grave apprehension. Even hoarseness at an early period of the maturative stage should be looked upon with suspicion.

Valuable information may often be gained by observing the nervous symptoms, especially at an advanced period of the disease. Great restlessness, insomnia, despondency, constant moaning, and grinding of the teeth in children are unfavorable symptoms. Violent and protracted delirium, convulsions, or coma usually preclude all hope of recovery. If, on the other hand, the state of the nervous system be tranquil and the patient passes quiet nights, has a contented disposition, and entertains a confident hope of recovery, the probability of a favorable termination of the disease is greatly increased, even though the eruption be severely confluent.

Even after a patient has passed safely through the perils of the regular stages of variola, his life may again be placed in jeopardy by certain complications. Fortunately, those which are most frequent—furuncles and abscesses—rarely lead to a fatal issue. The occurrence of pneumonia, pleuritis with effusion, erysipelas, or abortion should be viewed with deep concern. But the most fatal of the complications liable to arise are suppuration within the joints, septicæmia, pyæmia, empyema, and gangrene of the skin. When gangrene attacks the scrotum death, according to my experience, is inevitable.

Recovery from the hemorrhagic or malignant form of variola is scarcely to be expected. Mildly hemorrhagic cases of varioloid may occasionally progress to a favorable termination. Purpuric variola invariably ends fatally, and the fatal issue is rarely delayed longer than four to five days from the earliest symptoms.

PROPHYLAXIS.—There is no prophylactic measure against smallpox of so great importance as vaccination. In countries where this agent is carefully and systematically employed in infancy and repeated at the age of puberty epidemics of smallpox rarely if ever occur, and the deaths from that disease occupy a very low place in the mortuary tables. In view of the fact, therefore, that this very fatal and much dreaded disease may be prevented or modified and greatly limited in its spread by vaccination, it is highly important to a community that every individual should receive the benefits of this eminently protective agent. Gratuitous vaccination should be provided for the poor, and also for those who, through carelessness or indifference, would otherwise remain unprotected. Every unvaccinated person should be looked upon as a constant menace to the health of a community, inasmuch as he is liable to contract smallpox and disseminate the contagium ; hence the acceptance of vaccination should not be subject merely to the discretion of an individual whose judgment in regard to the matter may be warped by ignorance or prejudice, but should be made obligatory upon every citizen. But in the absence of any general statutory enactment very much can be done by local authorities to enforce vaccination by the adoption of certain restrictive measures. For example, no unvaccinated child should be permitted to attend school, public or private ; no child should be admitted into any institution for the care of children until vaccination has been performed ; no unvaccinated person should be enlisted in the army or navy or in the State militia ; and no unvaccinated immigrant should be permitted to land until vaccination has been properly performed.

If vaccination were generally practised in infancy and repeated as circumstances required, there would be but little need of considering any other means of protection against smallpox; but as it seems impossible to attain so desirable a result, it is necessary in the event of an outbreak of the disease to have recourse to other prophylactic measures. When a physician is called to a case of smallpox, his first duty is, of course, to vaccinate every member of the household in whom the operation has not been recently performed; next, he should, if possible, isolate the case. As isolation can only be accomplished with any degree of certainty by removing the patient to a special building or hospital, it follows that every city or town of considerable size should, at least in the event of an outbreak of smallpox, at once provide a well organized hospital, if none already exists, for the isolation and treatment of such cases. But if the patient must be treated at his home, every possible effort should be made to separate him from the rest of the family: only those who are required to act as nurses should enter the infected apartment, and they should be protected by recent vaccination. In selecting an apartment for the patient preference should be given to the room which is most completely separated from all other parts of the house. It should be well ventilated, and, if possible, have an open fireplace. All furniture which is not actually necessary for the comfort of the patients and attendants should be removed. While in attendance upon the sick the nurses should not come in contact with the other members of the family, and they should use every possible precaution in regard to cleanliness, disinfection of clothing, bedding, etc. A sheet wrung out in a strong solution of carbolic acid or, preferably, Labarraque's liquid, and suspended across the doorway, may aid in preventing the contagium from spreading to other parts of the house. During the illness of the patient the privileges of the well members of the household should be restricted. They should be advised not to attend church nor public assemblages of any kind. The children, if there be any, should at once be required to leave school, and should not be readmitted until the family physician or some qualified sanitary officer certifies that the sickness has ended, that the period of incubation has passed, and that the house has been thoroughly cleansed and disinfected.

Disinfection is highly important in preventing the dissemination of the variolous contagium. As the infecting principle clings to articles which have been used by the patient or which have been in the same apartment, all such articles as are worthless should at once be burned. All articles that can be laundried should be steeped for some time in some disinfecting solution, such as 2 fluidounces of chloride of zinc or 4 fluidounces of strong carbolic acid to a gallon of water, and afterward boiled for half an hour. For the disinfection of woollen goods nothing is equal to superheated steam. All utensils used by the patient in eating or drinking should each time be purified by boiling water. Even the secretions from the patient's mouth and nose or the excretions from his bowels should be disinfected by receiving them into a strong solution of chloride of lime or some other equally powerful germ-destroying agent.

The attendants upon the sick should not be more numerous than are actually required. Their clothing should be made of such material as can be readily boiled and laundried. Before associating with well persons they should take an antiseptic bath and change their entire clothing. The physician also should exercise great care lest he himself might be the means of spreading the infection. He should not remain in the sick chamber longer than is necessary to make a careful examination of the patient; his prescriptions should be written and the instructions given in another apartment. Before leaving the house he should take the precaution to wash his face and hands: the latter especially should be washed in some antiseptic solution. He should then delay visiting another patient until he has spent some time in the open air or, what is preferable, has changed his clothing. On entering the sick room he should not remove his overcoat nor even his hat; the former should be kept buttoned up to the chin. It would, of course, be safer to use a long rubber coat or linen duster, which should be kept hanging in the open air during the intervals of his visits.

The isolation of the patient should continue until all the scabs have fallen off and the skin has become quite smooth. Frequent bathing will aid in loosening the scabs, and the baths should be of an antiseptic character. Finally, the patient should not be permitted to associate with the public until his whole body has been washed with some disinfecting solution, such as a 1 : 2000 solution of corrosive sublimate or a 3 per cent. solution of Labarraque's liquid. The safest way of using either of these solutions is simply to sponge the body, carefully wet the hair, and then have the patient take a bath in plain water, with the use of soap. If he then be provided with clean clothing, no one need hesitate to associate with him, although his skin may be red and his face deeply scarred.

As the body of a patient who has died from smallpox is still capable of transmitting the contagium, certain precautions in regard to it are necessary. An effort should be made to disinfect the body by thoroughly soaking it with some powerful disinfecting solution. There is, perhaps, nothing more reliable than chloride of lime. Six ounces of this drug to a gallon of water makes a very effective germicide. The body should be wrapped in a sheet or blanket saturated with this or some equally powerful solution before it is placed in the hermetically sealed casket, and the burial should follow as speedily as possible, without, of course, a public funeral. From a sanitary point of view cremation of the corpse would be far preferable, but, unfortunately, this is for various reasons but seldom practicable.

The sick chamber and every article which it contains should be thoroughly disinfected after the room has been vacated by the patient, either by his recovery or death. This may be accomplished by burning in the room 3 pounds of sulphur to every 1000 cubic feet of air space, the room having first been made as nearly air-tight as possible. The disinfecting power of the sulphur dioxide will be greatly increased by the presence of moisture. As already indicated, all muslin and linen goods should be subjected to the boiling temperature for half an hour, and then laundried. Woollen clothing, pillows, mattresses, carpets, and all other articles which cannot be laundried should be so arranged in the room as to be thoroughly exposed to the influence of the sulphur dioxide, or else they should be conveyed to a disinfecting plant and exposed for two hours to either dry heat or superheated steam at a temperature of 230° F. After the apartment has been disinfected and cleansed it is advisable that it should remain unoccupied for two or three weeks, when it can be regarded as perfectly safe for occupancy.

TREATMENT.—In considering the treatment of smallpox it should be stated, first of all, that there is as yet no drug or agent known that is capable of exerting the slightest influence over the course of the disease after symptoms have once become manifested. But as scientific investigations are constantly adding to our knowledge important facts in regard to the causes of infective diseases, it is not improbable that before long we shall not only be able to recognize the specific cause of smallpox, but to antagonize its action. Until this new era arrives, however, we must continue to treat the patient rather than the disease, by addressing our remedies to the symptoms as they arise throughout the various stages of the disease.

During the incubation period of smallpox there are usually no symptoms requiring treatment. The only question to be considered at this stage is, Can anything be done to prevent or modify the approaching malady? Certainly no result can be expected from the use of drugs. What can be expected from vaccination? As the essential principles in the causation of variola and vaccinia are almost identical, it has been alleged that vaccination at this period of smallpox will hasten the variolous process, instead of modifying it. This view is extremely theoretical, and is certainly not based on experience. On the other hand, there are some who assert that hypodermic injections of vaccine lymph have produced good results. I would advise that this assertion be accepted *cum grano salis*. There are others, among whom may be mentioned Curschmann, who have never been able to see vaccination during the incubation stage exert any prophylactic influence whatever over the disease. My own experience is quite different. I have often seen smallpox greatly modified by vaccination after infection had occurred, and have not infrequently seen the disease prevented altogether.

It is my belief that when vaccinia has advanced to the stage of the formation of the areola around the vesicle it begins to exert its prophylactic power against smallpox. In perfectly typical cases this stage is reached about the eighth day. As the incubation period of variola is known to be from ten to twelve days, it is therefore quite possible for vaccinia to exert its protective influence in advance of the time when the earliest symptoms of smallpox should appear, provided that vaccination be not delayed too long after the infection has been received into the system. It may be said, in a general way, that the protection will be perfect or nearly so when the vaccine vesicle reaches the areolar stage in advance of any symptoms, and that in somewhat less advanced cases of vaccinia a modifying influence may be expected. As the modified form of vaccinia which results from revaccination is usually more rapid in its development, protection against the approaching disease in such cases may be expected with a greater degree of certainty than in those undergoing true vaccinia.

In endeavoring to prevent or modify smallpox at this stage it is of vital importance that the vaccine lymph employed should be fresh and active. Bovine lymph, as supplied to us on ivory points, is so often attended by failure, and, when it does succeed, its action is so slow, that dependence cannot be placed on it in cases where vaccinia has to compete with variola. In such cases I would advise the use of humanized virus when it can be procured, and especially that which has resulted from a long series of human transmissions. There is no virus more reliable or more certain to give prompt results than that taken from a typical vesicle on the eighth day. In using humanized virus it is important that several insertions should be made, as this will not only diminish the liability to failure, but, through the development of multiple vesicles, will bring the system more effectually under the vaccine influence.

During the initial stage nothing can be done to stay the progress of variola nor even to modify its course. The only thing that can be done is to endeavor to make the patient as comfortable as possible and to ameliorate special symptoms as they arise. The patient should be placed in a well ventilated bedroom in which the temperature is from 68° to 70° F. A light diet and cooling drinks are most appropriate. As the fever is usually high, febrifuge mixtures, such as liquor potassii citratis or liquor ammoniæ acetatis, containing a little spiritus ætheris nitrosi or tinctura aconiti, may be given in suitable doses at frequent intervals. A good combination is as follows:

℞. Spiritus ætheris nitrosi,
Syrupi limonis, *āā.* fʒiv;
Liquoris ammoniæ acetatis, f℥v.—M.
Sig. Give one to four fluidrachms, according to age, every two hours, in a little ice-water.

Phenacetin also will often be found very serviceable in doses of from two to three grains, every two hours, until several doses have been taken or until there is a reduction of the temperature. When there is irritability of the stomach the effervescing citrate of potassium is preferable to most other febrifuge mixtures. The swallowing of small pieces of ice is not only cooling in its effect, but is very useful when the stomach is irritable. When this symptom is very distressing, as frequently happens, such remedies as lime water, aromatic spirits of ammonia, subnitrate of bismuth, a little chloroform water, and the like may be used.

I have found nothing more serviceable in moderating a high temperature attended by a hot and dry skin than frequent sponging with cool water. At the same time, cold water, iced compresses, or the ice bag may be applied to the head. When this condition is present there need be no fear of suppressing the eruption by the use of cooling applications.

At this stage the nervous symptoms frequently demand treatment. For the relief of cephalalgia and lumbar pains, which are often distressing, large doses of some one of the bromide salts, caffeine, or phenacetin in doses of 5 or 10 grains, or, if preferred, some other analgesic of the coal tar series, may be employed. Convulsions, which are so common in children, may be relieved by warm baths or by giving internally bromide of potassium or hydrate of chloral. The latter drug is especially serviceable in convulsions, but care should be taken to

it well ted, as otherwise it will aggravate the throat symptoms.
n it cannot be swallowed it should be given by the rectum. These
gs are also very useful for the relief of insomnia and restlessness,
h so often demand attention. For these symptoms also Dover's
ler, when the stomach is not irritable, will often act well, or hypo-
ic injections of morphine and atropine may be given with good re-
s. Care should be taken not to apply sinapisms to any part of the
y for the relief of pain, as the irritation produced by them is very
tain to greatly increase the eruption on that particular surface, with-
diminishing it elsewhere.

fter the eruption has fully appeared the remedies just described
no longer required, as the fever now remits and the nervous symp-
s usually disappear. At this stage various drugs and other agents
e been recommended, and some of them from time to time highly
vaunted, as useful in modifying the eruption, but all have proved unavailing. Efforts have been made to accomplish this desirable result by the internal and external use of the various antiseptic or antizymotic drugs, such as carbolic acid, sulphocarbolate of sodium, salicylic acid, salicylate of sodium, xylol, and some others; but, while some writers strongly advocate their use, it must be said that none of these drugs have stood the test of experience. It has frequently been asserted that the exclusion of daylight from the bedroom is followed by good results. The same results, it is said, can be produced by excluding the ultra-violet rays, which have strong chemical action, by means of red window panes or by using red curtains tightly drawn around the bed. It is claimed by a recent writer that a patient thus treated will escape the stage of suppuration. I must, however, advise great skepticism in regard to this assertion. Those who are familiar with the history of smallpox will recall the fact that a similar treatment was introduced as far back as the time of Edward II. of England, whose son, it is said, was "treated for smallpox by being put into a bed surrounded with red blankets and a red counterpane, gargling his throat with mulberry wine, and sucking the red juice of pomegranates." It is perhaps unnecessary to make any further comment on this treatment than to repeat the very charitable criticism of Gregory, who said, "Let us, then, avoid the errors of our ancestors without reproaching them."

When the eruption is slow in making its appearance, as sometimes happens in children with a feeble circulation and a depressed condition of system, heat should be applied and hot stimulating drinks given. A bath quite warm, followed by enveloping the patient in blankets, is often very satisfactory in its results. Convulsions in this condition are very common, and when they occur demand the free use of the remedies already mentioned. As the eruption progresses to the vesicular stage there is always considerable burning and itching of the skin. This may be relieved to some extent by oleaginous applications. When there is very much swelling, especially about the face, arms, and hands, and the burning pain is severe, there is nothing that gives so much relief as frequent applications of cold compresses or cloths wrung out in cold water and kept constantly applied. For the intense pain frequently experienced in the palms of the hands, tips of the fingers, and soles of the feet cold applications, even iced compresses, are also very serviceable, yet I have seen rather better results follow the use of quite warm applications, such as warm hand and foot baths or hot poultices. If these agents fail and the patient is unable to sleep, opiates may be resorted to. A little morphine or deodorized tincture of opium often acts like a charm.

For the relief of the distressing symptoms resulting from inflammation and swelling of the mucous membrane of the mouth, fauces, and larynx, mouth-washes and gargles are required, such, for example, as solutions of chlorate of potassium, boric acid, tincture of myrrh, glycerole of tannin, and the like. The milder demulcent decoctions of flaxseed, gum arabic, and slippery elm bark will often be found decidedly palliative. I frequently use with much advantage flaxseed tea sweetened with white sugar and slightly acidulated with lemon juice. Ice cold lemonade is generally relished by the patient. Great relief is sometimes experienced by small pieces of ice being held in the mouth and allowed to dissolve slowly. Careful and frequent cleansing of the mouth usually affords considerable relief and enables the patient to swallow with greater ease. This may be accomplished by the nurse covering her index finger with a soft linen rag, dipping it into acidulated water or boric acid solution, and thoroughly cleansing the entire buccal cavity. If this be followed by spraying the mouth and fauces with a weak solution of cocaine, swallowing will sometimes be rendered easier in cases of dysphagia.

The nervous symptoms are frequently so prominent during the eruptive stage as to demand treatment. Such symptoms as persistent insomnia and violent delirium are most common. Not infrequently this condition is attended by a flushed face and bounding pulse, in which case a saline purge and an ice bag to the head may be of service. Sulphate of morphine and tartar emetic, in doses of ¼ grain of each, repeated every two hours until a few doses have been taken, will frequently quiet the delirium and produce sleep. Of course some one of the bromides and hydrate of chloral are to be preferred in the larger proportion of cases. Care must be taken, however, not to use narcotics too freely, lest the patient lapse into coma or sink into collapse. When the delirium is violent or maniacal, it will be necessary to use some means of physical restraint to prevent the patient injuring himself or others, especially if he be large and muscular.

Smallpox is by far most fatal during the stage of suppuration. The chief indications for treatment at this stage are to mitigate the suppurative fever, to disinfect the exudation from the pustules, and to oppose by every possible means the tendency to death from exhaustion. If the patient can be carried safely through this stage and the early part of the stage of desiccation, his recovery may be reasonably expected, unless some serious complication should arise.

When the temperature is very high the ice bag should be kept on the head and sponging with cool or tepid water resumed. In warm weather the temperature of the patient may sometimes be reduced by covering him with a sheet wrung out in cool water and renewing it every few minutes. Occasionally cold applications are not well borne, in which case tepid water may be tried. Cool immersion baths have not met with anything like the same results in variola as in typhoid fever. Some one of the antipyretics of the coal tar series will often be found useful. I have frequently used phenacetin, in doses of 2 or 3 grains every two hours until several doses have been given, with good results. When this drug, however, is discontinued the fever usually recurs, but during the short interval from intense fever the patient is often able to take a little more nourishment than he would otherwise do, and sometimes enjoys an hour or two of refreshing sleep. On account of the depressing effect occasionally seen from the use of these drugs it is advisable to give stimulants at the same time.

To allay the intolerable itching and to correct the offensive odor resulting from decomposition of the purulent material that exudes from the pustules certain local applications will be found of great service. Antiseptic washes may be used, such as a solution of boric acid (1 : 20), of carbolic acid (1 : 100), or of bichloride of mercury (1 : 2000). When the odor is highly offensive great benefit may be derived by keeping the patient's face, hands, and other parts of the body, if necessary, constantly mopped with a solution of hypochlorite of sodium. I frequently use with advantage a 5 per cent. solution of Labarraque's liquid, directing that not only the patient, but the bedding also, be sprayed every little while by means of an atomizer. Various antiseptic oleaginous preparations are also useful. There is nothing more convenient and, upon the whole, more serviceable than equal parts of olive oil and lime water containing a little carbolic acid or oil of eucalyptus. This should be applied freely three or four times a day with a large camel's hair brush. I have been using lately with considerable benefit an ointment composed of aristol 15 or 20 parts to 100 parts of vaseline. Two drachms of liquor sodæ chloratæ to an ounce of lard are also serviceable. Likewise I have used with advantage antiseptic dusting powders, such as 15 parts of aristol to 100 parts of talc or powdered starch.

It is, I think, scarcely necessary to speak at length of the various means which have been recommended from time to time for the prevention of pitting, for not even the highly vaunted methods when put to a critical test have been found worthy of the praise given them. To accomplish this purpose it is necessary that the pustular stage of the eruption should be either prevented or greatly modified, for the suppurative process is always attended by destruction of derm tissue, and any loss of this tissue is inevitably followed by scarring. After considerable experience with many of the most highly lauded ectrotic measures, so called, I have come to the same conclusion as Gregory, that there is no peculiar method yet known for the prevention of pits and scars: "The masks and ointments formerly in use for that purpose, and so highly vaunted, are, in reality, more hurtful than beneficial." A little cold cream, vaseline, benzoated lard, or lanolin, containing some antiseptic, is all that can be recommended.

As the vital powers of a patient suffering from confluent variola are severely taxed during the stage of suppuration, it is important that a supporting plan of treatment should be adopted. This is quite obvious when we consider how great the quantity of purulent material generated must be. Watson has estimated that it amounts to quarts. Besides this excessive strain upon the system, the vast irritation resulting from inflammation of almost the entire cutaneous integument is very exhausting in its effects, being comparable only to that which results from an extensive burn. The first evidence of flagging of the vital forces is usually a sudden subsidence of the swelling and redness of the face and hands, causing the skin to become pale and the pustules to shrink or present a collapsed appearance. If this condition continues, the pulse becomes rapid and feeble, the tongue brown and dry, and subsultus tendinum, general tremors, and delirium rapidly supervene. It is advisable to anticipate these symptoms by the early employment of supporting measures. When maturation of the pustules begins the patient should receive a liberal amount of nutrients and stimulants. Milk, peptonized if necessary, should be given at frequent intervals. I usually insist that an adult patient suffering from a severe form of variola shall receive during each twenty four hours from 2 to 3 quarts of unskimmed milk, 2 to 3 raw eggs, and 6 to 12 ounces of good whiskey, the latter being given in the form of milk punch. The eggs may be well beaten and drank with the milk or they may be given in the form of eggnog. It is important that these supporting agents should be faithfully continued during the night as well as the day, for when prostration is extreme the tendency to sink into collapse seems greatest between midnight and morning. When milk and whiskey cannot be taken in sufficient quantity, or when there is great repugnance to these articles, bouillon with eggs, a well prepared beef tea, nutritious broths, and a liberal amount of wine may be given instead. As a stimulant in cases of profound prostration Curschmann esteems very highly the Stokes cognac mixture, prepared as follows:

℞. Cognac optimi,
Aquæ destillatæ, *āā.* fʒxv;
Vitelli ovi, No. i.,
Syrupi, fʒvj.—M.
Sig. Give a tablespoonful at frequent intervals.

Usually but few drugs are required at this stage of the disease. The less the stomach is taxed with the ingestion of drugs, and the more completely its labor is limited to the important function of sustaining the vital forces and the nutrition of the body, the greater will be the chances of recovery. If the bowels should be confined, rather than give purgatives, enemas should be used. Sulphate of quinine is usually serviceable in tonic doses. When the heart action is weak, sulphate of strychnine and digitalis will be found most useful. Carbonate of ammonium is also useful in cases of threatened cardiac failure. In case of great restlessness and insomnia narcotics may be cautiously given hypodermically or by the rectum. The occurrence of diarrhœa should receive prompt attention.

In cases of varioloid usually very little treatment is required after the initial stage has passed, as this form of the disease rarely ends fatally. On the other hand, hemorrhagic variola almost always terminates fatally in spite of the best treatment. The drugs usually employed are the mineral acids, ergot or ergotin, sulphate of quinine, and tincture of the chloride of iron, together with the external use of styptics and cold compresses; but these agents are recommended, I regret to say, in conformity with general usage than with any expectation of ng a cure. Transfusion has also been tried, but the results have en encouraging.

e various complications liable to arise should be treated on general ples, according to their nature and the indications presented. Fu- es and abscesses should be opened as soon as they form, and the especially should receive antiseptic treatment. An effort should de to prevent the occurrence of the serious forms of eye compli- ns by washing from the conjunctiva all purulent material as fast as ms. This may be accomplished by carefully injecting under the solution of boric acid (10 or 15 grains to an ounce of water), using ll syringe or dropper. The eyes should be carefully watched, and a corneal ulcer appears it should at first be treated by the appli- n of cold compresses. Besides thorough cleansing a solution of 10 15 grains of boric acid and 2 to 4 grains of atropine to an ounce of stilled water should be instilled into the eye once or twice daily. I ve occasionally touched the ulcers very delicately with a stick of itrate of silver brought to a fine point, as recommended by some authors, but with no decided benefit. Indeed, in spite of treatment, the ulcerative process too often continues until the vision is entirely destroyed.

Convalescence from smallpox may be hastened by tonics and a liberal diet. The compound tincture of cinchona is useful at times to increase the appetite, although, as a rule, convalescents eat heartily. In cases of great emaciation and exhaustion iron, cod liver oil, and the malt uors are very useful. If there should be a constant occurrence of ils or a furuncular diathesis, some benefit may be derived from the administration of Fowler's solution or sulphide of calcium. The separation of the scabs may be hastened by the free use of glycerin or cosmoline and warm baths. If warty nodules remain on the face after the scabs have fallen off, their removal may be hastened by touching them once or twice daily with tincture of iodine.

VACCINIA.

BY WILLIAM M. WELCH, M. D.

SYNONYMS.—Latin, Vaccinia or Variolæ vaccinæ (Jenner); English, Cowpox or Kinepox; French, Vaccine; German, Kuhpocken, Impfpocken, or Schutzblättern; Italian, Vaccina; Spanish, Vacuna.

DEFINITION.—Vaccinia is a disease communicable only by inoculation, and is characterized by one or more skin lesions, according to the number of insertions of the specific virus, running through the stages of papulation, vesiculation, and pustulation, ending in desiccation and falling of the crusts at the end of the third week. The process is attended by very little if any febrile reaction, and, when completed, confers immunity against smallpox.

HISTORY.—Toward the middle of the eighteenth century an impression arose among the common people employed in the dairies of England that a certain disease of cows known as cowpox would, when accidentally communicated to the milkers, afford them protection against smallpox. This belief gradually increased until, at length, in 1774, a Gloucestershire farmer, named Benjamin Jesty, became so fully convinced of the prophylactic power of cowpox that he ventured to inoculate his wife and two sons with, presumably, some of the virus from the teats of a cow suffering from the disease. But the subject received no scientific consideration until it attracted the attention of Edward Jenner, a country physician of Berkeley, England, where dairy farms were numerous. When he was yet a medical student, Jenner's interest was elicited in the matter by hearing a countrywoman remark that she could not take smallpox because she had been infected with cowpox. Later, when a practitioner of medicine, he took great pains to inquire into the facts upon which this tradition was founded, and he soon became convinced that there was a reality about it; but, setting a good example to all investigators, he continued his researches for several years, and demonstrated most conclusively the value of his discovery before publishing his observations to the world.

The first practical demonstration of the new inoculation, as it was called, was made by Jenner, May 14, 1796, in a peasant lad named James Phipps, aged eight years, whom he inoculated with virus taken from a vesicle on the hand of a dairymaid, who had been accidentally infected by milking a cow affected with cowpox. Wishing to test the protective efficacy of the vaccine disease, Jenner tried, on the first day of July following, to give this lad smallpox by inoculating him with variolous matter, but failed. He repeated the test several months later with the same negative result. After continuing his investigations for two years longer, and accumulating a mass of evidence that was simply incontrovertible, Jenner published, in London, June, 1798, his observations in a paper entitled "An Inquiry into the Causes and Effects of the Variolæ Vaccinæ, etc."

It must not be supposed that the great and important truth promulgated in this paper was accepted without opposition. On the contrary, it was doubted by some and ridiculed by others. Some, indeed, carried their opposition so far as to attack the honesty and veracity of Jenner. Still others, even more bitter in their opposition, caricatured the effect of the inoculation by representing man transformed into a horrid monster presenting some of the characteristics of both man and the bovine animal. But the force of Jenner's facts was such that, in spite of this detraction, it was not long until his discovery was known and welcomed in every civilized country in the world, and the experience of a century affords a most complete confirmation of all that was claimed for it by its discoverer.

The new inoculation was introduced into America by Benjamin Waterhouse, the first professor of the theory and practice of medicine in Harvard College. The first person subjected to its influence was his eldest son, aged five years. This occurred July 8, 1800. Observing that the vaccinia in this child passed through the regular course, as described by Jenner, he took virus from this case and with it inoculated the rest of his children. After the vaccine disease had run its course, he proceeded to test its efficacy against smallpox by taking his children into the smallpox hospital and exposing them freely to the contagium of that disease. Finding they resisted the contagium in the natural way, he had them inoculated with variolous matter. This also failed to produce the disease. He then very truly remarked, "One fact, in such cases, is worth a thousand arguments." It is instructive to add that Waterhouse was greatly aided in his work of introducing the new inoculation in this country by Thomas Jefferson, then President of the United States. It was largely through his efforts that the virus of vaccinia was speedily disseminated throughout the Southern and some parts of the Middle States.

As the result of Jenner's discovery the spread of smallpox has everywhere been greatly controlled and the mortality from that disease enormously diminished. In England and Wales, where the registration records are perhaps more complete than in most countries, it was found that before the introduction of vaccination the annual mortality from smallpox was at the rate of 3000 deaths in every million of the population. Since the adoption of this protective measure the ratio of deaths to the population from that disease has constantly diminished. According to Moore,[1] only 15 deaths were caused by smallpox in England during the year 1890. While this, undoubtedly, is an unusually small number, yet during the ten years from 1881 to 1890, inclusive, the average annual rate of mortality from that disease was only one seventieth part of what it was during the pre-vaccination period. Furthermore, it has been found that where vaccination in infancy has been carefully and systematically practised, as in Germany, for example, the mortality from smallpox among children, instead of being enormous, as formerly, has become almost *nil*.

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[1] *Text-Book of the Eruptive and Continued Fevers.*

The protection conferred by vaccinia has not only greatly diminished the number of cases of smallpox, but has very considerably reduced the death rate among those attacked. Moore[1] gives statistics which show that in Sheffield, during the outbreak of 1887–88, of 4151 vaccinated patients 200 died, a death rate of 4.8 per cent.; while of 552 unvaccinated patients, 274 died, a death rate of 49.6 per cent. A report by Grimshaw of Dublin on the unusually widespread and malignant epidemic of smallpox which occurred in 1871–72 shows the comparative death rate in several hospitals among the vaccinated and unvaccinated patients to have been as follows: In Cork Street Hospital, of vaccinated patients, 10.8 per cent. died, and of the unvaccinated, 71.8 per cent.; in Hardwicke, 11.2 per cent. of the vaccinated, and 78.57 per cent. of the unvaccinated; in Cork, 5.5 per cent. of the vaccinated, and 58 per cent. of the unvaccinated; in London Smallpox Hospital 14.9 per cent. of the vaccinated, and 66.2 per cent. of the unvaccinated; in Hampstead (London), 11.4 per cent. of the vaccinated, and 51.2 per cent. of the unvaccinated; in Homerton, 5.9 per cent. of the vaccinated, and 37.7 per cent. of the unvaccinated.

It has been very clearly shown that the degree of vaccinal protection is proportionate to the perfect evolution of vaccinia. Marson and others of large experience have found that smallpox is less fatal among patients who bear unmistakable evidence, in the form of typical scars, that the vaccine disease had run a perfect course. While Jenner never said very much about the character of the scar, he nevertheless constantly insisted that the vaccinal process should observe a certain definite course, which he carefully described, in order that the protection should be perfect. As tending to show that the degree of protection can be measured to a considerable extent by the quality of the vaccine scars borne by persons, the writer presents the result of his own experience in the following table:

	Cases.	Deaths.	Percentage of deaths.
Vaccinated in infancy—good scars	1474	124	8.41
" " —fair scars	701	101	14.4
" " —poor scars	1104	296	26.81
Post-vaccinal cases	3279	521	15.88
Unvaccinated cases	1926	1059	54.98
Unclassified cases	116	25	21.55
Total	5321	1605	30.16

ETIOLOGY.—It is generally believed that vaccinia, etiologically considered, is closely related to variola. Jenner was evidently of this opinion when he applied to it the name variolæ vaccinæ. The disease as it occurs in the cow has been thought to be in reality smallpox robbed of its virulence by passing through the system of the bovine animal. This theory has led a number of very able investigators to attempt to produce cowpox at will by inoculating cows with variolous matter. Among the names of such investigators may be mentioned as most prominent those of Ceely, Reiter, Badcock, Thiele, and Voigt.

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[1] *Loc. cit.*

Some of these men present strong claims of success, while others have unquestionably failed, and, even worse than that, have inoculated variola back into the human subject by using the virus from a vesicle raised by variolating the cow. Reiter met with this unfortunate result, and so also have some other experimenters. The writer must therefore advise great skepticism in regard to the assertions that vaccine virus may be produced at will by this method. Under no circumstance should such virus be inoculated into the human subject until it has passed through, so to speak, a series of bovine animals and the local process has been found by close and careful comparison to be identical with that of undoubtedly true vaccinia in the heifer.

Vaccinia usually occurs in the human subject as the result of intentional inoculation with a strain of virus that was originally taken from a cow suffering from what is commonly called spontaneous cowpox. This term is not intended to imply that the disease develops in the cow independently of contagium, but rather that it appears without any known source of origin. This affection is believed to have been more prevalent among cows in Jenner's time than at present. When once the disease was introduced among a herd of cows on a dairy farm it was found to spread from one to another, and thus continue for months, and even years, if new stock were continually added to the herd. As the disease was particularly prone to attack heifers during their first lactation, it is evident that the infection was principally conveyed from one cow to another by the hands of the milker. It is doubtful whether the disease ever spreads among bovine animals in any other way than by inoculation. By this means cowpox may be communicated from one bovine animal to another through an indefinite series, and the supply of vaccine virus thus produced need be limited only by the demand or the number of animals inoculated. It is well known to the propagators of bovine virus that the disease cannot be communicated a second time to the same heifer.

Jenner's theory of the origin of cowpox was that it results from grease in the horse. It must not be understood that he ascribed the origin of cowpox to the ordinary eczematous affection that so commonly occurs in horses' heels as the result of uncleanness, and called "grease" by hostlers, but to a rare and peculiar form of eruptive disease described by the French as *eaux aux jambes*. He believed that cowpox was due to the accidental conveyance of the virus of grease to the teats of a cow by a milker whose business was also to care for horses' heels when affected with that disease. Jenner admitted, however, that he was not able to prove the correctness of this opinion by "actual experiments conducted immediately under his own eye," but believed that the evidence he collected was sufficient to establish it as a fact. It is not improbable that the grease spoken of by Jenner was in reality a localized eruption of equina, or horsepox, for such a disease is said to exist among horses. Depaul claimed he had demonstrated that this affection was capable of giving rise to cowpox in the cow by inoculation. But, after all, it must be said that while Jenner's theory has not been disproved, it has not been fully confirmed, and that the theory that regards spontaneous cowpox as a disease *sui generis* in the bovine animal is probably correct.

It seems probable that there is in the vesicles of vaccinia some special bacillus which acts as the infecting principle, but thus far none has been described. The only micro-organisms seen that are at all liable to serve as the infecting agents are certain cocci, but there is nothing peculiar about them ; they cannot even be distinguished from the bacteria found in the vesicles of variola.

PATHOLOGICAL ANATOMY.—The lesions of vaccinia are limited to that part of the skin where the vesicles develop. At the point of inoculation of the vaccine virus the papillary layer of the derm at first becomes congested, and in the course of three to five days a slight inflammatory action is set up, followed by an exudation of lymph. As the lymph increases, the epidermis is detached and lifted from the other layers of the skin, and forms the roof or upper covering of the vesicle. The squamous cells of the epidermis are not entirely destroyed by the accumulation of lymph, but are stretched and forced out of their normal relation to each other, so as to form cavities, or rather partition walls, within the vesicle. It is a well known fact that the vesicle is not unilocular, but multilocular ; hence it cannot be entirely emptied nor destroyed by a single puncture.

The lymph at first is thin and pellucid, but later it becomes opaque and viscid. Examined microscopically, it is found to be a mixture of fibrin, corpuscular elements, and, as the process advances, certain detritus from tissue changes, and even pus corpuscles. In addition to this a large number of small spherical bodies, or micrococci, may be seen, and these constitute, as is generally believed, the virulent element of the lymph. In the human subject the lymph is clearer, more limpid, and more soluble than in the animal, and hence that from the former may be used for transmitting the vaccine disease with greater certainty of success.

A slight depression, termed umbilication, is usually seen in the vesicle, even at an early stage of its development. If carefully examined, it will be found that the centre of the pock where the depression exists has already undergone desiccation ; this prevents central distention of the vesicle, so that growth takes place by peripheral enlargement. As the process of evolution advances, the deeper layers of the skin become involved and its connective tissue suffers by inflammatory and ulcerative action. In some cases the inflammatory action even extends to the subcutaneous tissue or may give rise to a necrotic condition of the skin. But all results of this kind when excessive should be regarded as inflammatory complications rather than as essential features of true vaccinia.

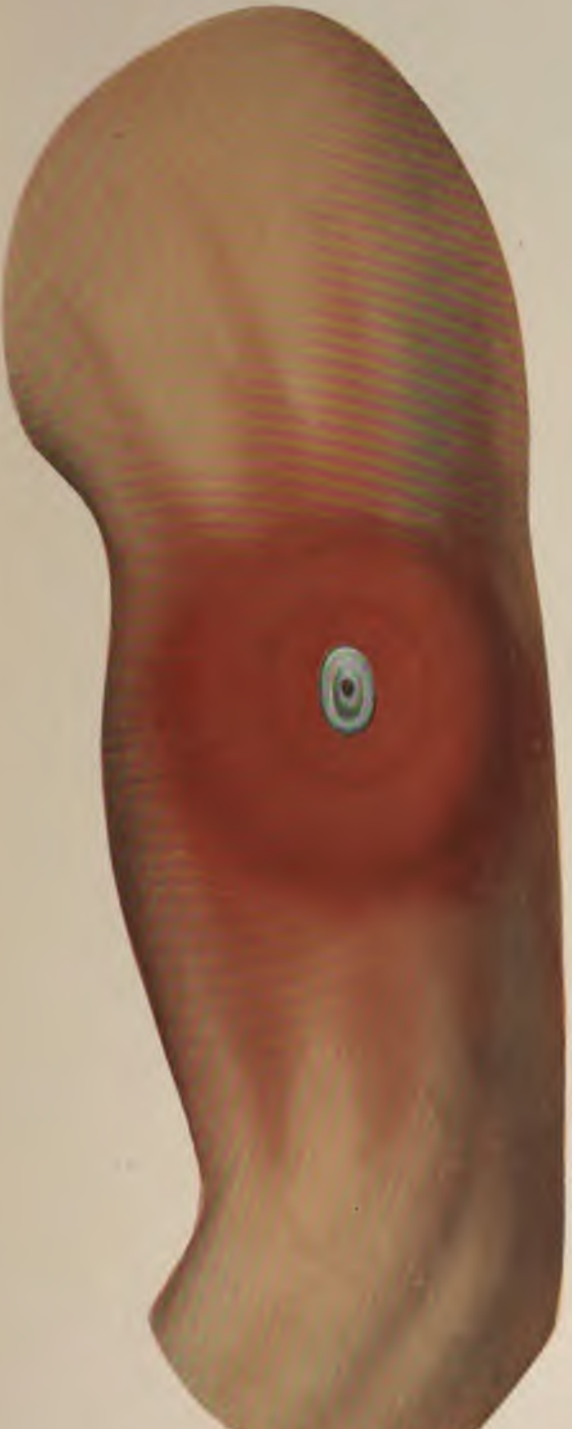
The scab which forms as the ultimate result of the evolution of the pock shows, when examined microscopically, not only the organisms already mentioned as present in the lymph, but also blood corpuscles, pus corpuscles, broken-down epithelium, and other débris. As a sequence of the destruction which has taken place in the connective tissue elements of the deeper layers of the skin a permanent cicatricial lesion remains. The cicatrix is to a great extent peculiar and quite characteristic. One that is perfectly typical presents well defined margins, is reticulated or foveolated, and, without much stretch of the imagination, looks as if it had been stamped into the skin by a sharply-cut die. It has been said that genuine pocks are frequently not folved by scars, but, without denying this absolutely, the writer would advise that such assertions should be regarded with some degree of skepticism.

SYMPTOMS AND COURSE OF THE DISEASE.—Vaccinia in the human ject, as already stated, is always produced by inoculation. During first two or three days after the insertion of the vaccine virus no mptoms are observed beyond those incident to the slight abrasion the skin made by the operator's knife. On the third or fourth day ery faint redness may be seen around the site of the inoculation. This edness gradually increases, while at the same time a distinct papule is formed, which becomes slightly more prominent by increasing in area ather than height. On the fifth day the lesion begins to assume a esicular condition. This is usually seen first at the margin of the seat of inoculation. The vesicle gradually increases in size, and the lymph that it contains is at first thin and perfectly transparent. On the eighth day the vesicle reaches its greatest perfection: it is then considerably elevated above the surface of the skin, and presents a pearly or yellowish appearance. When examined closely it will be found to have, even at an early stage of its development, an umbilicated form similar to that seen in the vesicles of variola. About this time there appears around the vesicle an inflammatory circle which is called the areola. During the ninth and tenth days the redness increases and the inflamed skin becomes tense and painful, and streaks of redness often extend a considerable distance from the lesion (Plate IX). When the action is intense a few papillary elevations appear near the vesicle. Occasionally the cellular tissue becomes involved in the inflammatory action. Frequently, indeed, the glands of the axilla swell and become painful, provided that the inoculation has been done, as is customary, on the arm.

At the same time mild constitutional symptoms appear. Slight rigors sometimes occur, followed by very moderate elevation of the temperature. It is not often that the temperature rises more than one or two degrees above the normal. There are apt to be malaise, impaired appetite, and disturbed sleep; but none of these symptoms continue very long. In recording very carefully the constitutional disturbance observed in his first case of induced vaccinia, Jenner says: "On the seventh day he (a boy aged eight years) complained of uneasiness in the axilla, and on the ninth he became a little chilly, lost his appetite, and had a slight headache. During the whole of this day he was perceptibly indisposed, and spent the night with some degree of restlessness, but on the following day he was perfectly well." It cannot be doubted, however, that many children pass through the regular course of vaccinia without any apparent systemic disturbance; while, on the other hand, it sometimes happens, especially in secondary inoculations, that the symptoms, both constitutional and local, are very severe. It occasionally happens in severe cases of primary vaccinia that a cutaneous eruption appears at this stage of the disease. This eruption consists of numerous maculæ similar to measles, and covers almost the entire body. On account of its comparatively frequent association with the vaccine process it has been called *roseola vaccinosa*. It seldom continues longer than two or three days. Fever, of course, accompanies this symptom.

On the eleventh or twelfth day the pock begins to fade. In its declin-

PLATE IX.



Vaccinia on the Tenth Day.

ing stage its contents become opaque, desiccation appears in its centre, and the areola shades off into two or three concentric circles, varying in color from a pale red to a deep red or livid tinge. By the fifteenth day desiccation is usually completed, although the crust does not fall off nor can it be easily removed until the end of the third, and frequently not until the end of the fourth, week. The completed crust is of a mahogany color, rough on its exterior, thin at it centre and periphery, with a thick circular ridge between. The scar is at first red, but in the course of a few months becomes paler than the surrounding skin. It is pitted or foveolated, and not unfrequently presents radiating bands or striæ of cicatricial tissue.

As the analogy between cowpox and smallpox is in most respects very close, and as variola frequently differs in the duration and severity of its local manifestations, so also it must not be expected that the local lesions of vaccinia will invariably follow the typical course just described. In some cases the course of the disease is undoubtedly shorter and milder, while in others it is longer and severer. No deviation, however, should occur in the evolution of the pock; that is to say, it should pass through the stages of papulation, vesiculation, and pustulation. The vesicle may be delayed in making its appearance or tardy in its development. It has been known to appear as late as one month after the inoculation was done, and then develop and run regularly through its course. Likewise the constitutional symptoms are not uniform; they may not be present at all, or, if present, are so mild as to pass unobserved.

Passing over the numerous irregularities of the vaccine lesion described by the earlier writers, it is deemed necessary to refer only to a single spurious variety which has grown more frequent of late years—namely, the red raspberry excrescence, as it is commonly termed. This growth, when seen, usually appears from three to seven days after the introduction of the virus, beginning as a red elevation at the site of inoculation, quite similar in appearance to the papule of true vaccinia, but instead of advancing to the vesicular stage it remains hard, dense, bright red in color, and nodular in form, looking not unlike a small nævus. A thin fragile crust forms on its surface, but when this is removed the lesion continues to present the same general appearance just described. It is very persistent, remaining usually for weeks or even months; no areola forms around it at any time, and it is not followed by a scar.

This peculiar excrescence was described by some of the earlier writers on vaccination, but during the long period in which humanized virus was used exclusively it was not observed. Since the introduction and general employment of animal vaccine virus it has frequently been seen. It seems therefore that it occurs as the result of inoculating the human subject with some unknown form of inert or non-specific material taken from a vaccinated bovine animal. That this is a spurious form of the vaccine disease, and utterly devoid of protective power against either variola or vaccinia, the writer has had ample opportunities of proving.

COMPLICATIONS AND SEQUELÆ.—The complications liable to rise in the course of vaccinia are not numerous. Those due to excessive inflammatory action of the skin are most common; but they usually occur as the result of undue traumatism, or injury to the pock and the accidental introduction of septic material, or some pre-existing cutaneous disease, or some dyscrasia. In children with a strongly marked scrofulous diathesis, lymphangitis and lymphadenitis, more or less severe, not unfrequently result. Likewise, where there is a tendency to eczema, that affection sometimes follows the maturation of the pock. In the early days of vaccination it was thought that any existing cutaneous disease, however mild, was not only liable to be aggravated by vaccinia, but that its presence was likely to interfere with the most perfect development of the vaccine lesion. This belief, the writer thinks, is not altogether warranted by experience. It is, of course, desirable that a child should be free from any disease whatever when vaccinated, but when there is danger of variolous infection no cutaneous disorder, not even that resulting from the acute exanthemata, should interfere with the prompt performance of the operation.

There are a few diseases of a specific character that may be transmitted by vaccination, especially when proper care is not exercised. *Impetigo contagiosa* is said to have been communicated by the use of a vaccine crust taken from a person in whom that disease coexisted with vaccinia. *Erysipelas*, also, has been known to follow vaccination, but it must be admitted that this is a rare complication at the present day. The writer is familiar with a few instances in which it occurred many years ago as the result of carelessly using decomposed humanized crusts. It is generally believed, however, that the more frequent source of erysipelas is secondary infection, resulting from the presence of the contagium of that disease in the surroundings of the patient.

Of all possible complications, the most serious is *syphilis.* For a long time it was doubted whether this disease could be communicated by vaccination, but since the careful study of the subject and of cases by M. Viennois of France and Jonathan Hutchinson of England the truth of the matter has come to be recognized by the profession generally. It was at first thought possible to convey syphilis by vaccination only when vaccine lymph was taken from syphilitic subjects in such careless manner as to permit of its contamination by blood, but it has been shown by Ricord and Jonathan Hutchinson that vaccine lymph is never entirely free from blood.

While, therefore, it is possible to transmit this dreaded disease in this way, the danger has been greatly exaggerated. It has fallen to the lot of but few to see cases of vaccino-syphilis. It is a well known fact that the inherited form of the disease usually manifests itself during the first two or three months of infantile life; therefore, by carefully observing the health of the infant, and declining to take virus from any child under four months of age, the risk of communicating syphilis by vaccination would be entirely *nil.* Besides, it is easy now to allay the fears of the most timid in regard to this matter by the employment of vaccine lymph from the heifer, since that animal is known to be insusceptible to syphilis.

There are only two sequelæ that follow vaccinia—one is immunity from variola, and the other is the scar. The scar is usually characteristic, but in very exceptional cases the writer has known it to assume the appearance of a keloid growth. In these cases bovine virus had been employed.

THE TECHNIQUE OF VACCINATION.—*Humanized Virus.*—Previous to the introduction of animal vaccination in this country and the propagation of bovine lymph humanized virus was employed exclusively. In Jenner's time it was the habit to use this virus in the form of lymph from the vesicle. Jenner believed that only the superficial lymph should be employed, while others contended that it should be taken from the floor of the vesicle. Time, however, has shown that the lymph from all parts of the vesicle is equally efficient. The time of taking the lymph is undoubtedly of much greater importance. Experience has long since shown that the proper time to take it is from the fifth to the eighth day, since at a later period it is quite sure to become mixed with inflammatory products. No lymph should be taken after the formation of the areola. Jenner's instruction on this point was very explicit and emphatic, and indeed considered so important that it was called the golden rule of vaccination. It was this: "Never to take the virus from a vaccine pustule for the purpose of inoculation after the efflorescence is formed around it. I wish this efflorescence to be considered as a sacred boundary over which the lancet should never pass."

No form of virus is more certain to succeed, and surely none gives better results, than fresh lymph taken from a vesicle on the eighth day of its development. This will often succeed in producing vaccinia after every other variety of virus has failed. Unfortunately, the lymph does not retain its virulence very long in a dried state, except in the form of crust, and arm-to-arm vaccination, which is the most successful method of using it, is but rarely practicable in this country. Attempts have been made to preserve the lymph in capillary tubes hermetically sealed, but it has been found that its virulent property is difficult of preservation in this way. The crust is the only form of humanized virus that is readily accessible or that can be depended on when it is necessary to preserve it for a long time. Formerly the crust was the common source of vaccine supply, but it has been supplanted almost entirely by vaccine lymph from bovine animals. Direct observation, however, has fully convinced the writer that the former virus, especially that which has been long humanized, is far more trustworthy than the latter as a prophylactic agent after exposure to the contagium of variola. This is not only because of the well known fact that humanized virus succeeds more readily than the bovine lymph usually found in the market, but also because it is prompter in its action, produces a vesicle that reaches maturity earlier, and thus affords speedier protection.

Animal Vaccine.—By animal vaccine is meant the vaccine that is produced in calves or young heifers by the continued propagation of virus taken originally from a case of spontaneous cowpox. It is necessary to consider only three forms of this vaccine—the liquid lymph, dried lymph, and the crust. The liquid lymph is active when it can be used direct from the calf, but when stored in capillary tubes it soon loses its virulence. Some crusts are active, but most of them are inert. Besides, they contain a good deal of débris and matter liable to undergo decomposition; hence they should never be used. The dried lymph, therefore, is the form generally employed, and this is usually served to the profession on ivory points, sometimes on slips of quills. It should be kept cool and free from moisture.

In performing vaccination the upper layer of the skin should be slightly abraded, so that the virus may be brought in contact with the absorbents. This may be done by means of an ordinary lancet or an ivory point containing the bovine lymph. An instrument not too sharp is preferable for the operation, as the horny layer of the cuticle should be scraped or scratched rather than incised. Too much oozing of blood is undesirable. Immediately the virus should be well rubbed on the abraded surface. If dried vaccine from the bovine animal be used, it should first be perfectly dissolved. In using humanized virus in the form of a crust or scab, a small fragment should be cut off and crushed to a fine powder between two pieces of glass, such as microscope slides, then moistened with sterilized water and brought to the consistence of mucilage. Of course the skin of the patient at the site of the inoculation should be properly cleansed with some antiseptic solution before the operation, and the lancet sterilized.

Apart from the objection arising from the presence of the scar, it is not important on what part of the cutaneous surface the inoculation is done. The region most frequently selected is the arm near the insertion of the deltoid muscle. This part is easily accessible, while at the same time it is comparatively free from muscular contraction and lymphatic glands. After the operation it is advisable to keep the arm bare for a few minutes. The practice of applying court plaster should be condemned. To avoid irritation from the clothing there is no objection to using some one of the shields devised by instrument-makers, although they are not usually required.

	Cases.	Deaths.	Percentage of deaths.
Unvaccinated	1668	909	54.49
Claiming to have been vaccinated; no visible scar	258	150	58.13
Vaccinated from one to seven days before the appearance of the variolous eruption	59	25	42.37
Vaccinated longer than seven days before the variolous eruption appeared	95	17	17.89
Vaccinated in infancy—one good scar	820	70	8.53
" " " — " fair "	451	70	15.52
" " " — " poor "	874	256	29.29
Total number showing one scar	2145	396	18.46
Vaccinated in infancy—two good scars	287	20	6.97
" " " — " fair "	114	14	12.28
" " " — " poor "	102	24	23.53
Total number showing two scars	503	58	11.53
Vaccinated in infancy—three good scars	122	10	8.19
" " " — " fair "	49	4	8.16
" " " — " poor "	51	13	25.49
Total number showing three scars	222	27	12.16
Vaccinated in infancy—four or more good scars	251	24	9.56
Vaccinated in infancy—four or more fair scars	81	10	12.34
Vaccinated in infancy—four or more poor scars	97	11	11.34
Total number showing four or more scars	429	45	10.49

The opinion has been advanced, more especially by Marson of London, that the degree of vaccinal protection in an individual is directly proportionate to the number of insertions made. This opinion was based upon his very extended experience with smallpox, in which he found that the disease was less severe and less fatal in proportion to the number of vaccine scars borne by each patient. According to his statistics, the death rate among patients showing one scar was 7.5 per cent., two scars 4.125 per cent., three scars 1.75 per cent., four or more scars 0.75 per cent. Among those presenting uniformly typical scars the death rate was still less. The writer's experience on this point does not entirely agree with that of Marson's, as may be seen in the preceding table.

According to the writer's experience, the *quality* of vaccine scars is a far more reliable indication of the degree of protection than the *quantity*. The table shows that when the scars are typical it makes no difference whether they are single or multiple, the protection being practically the same. There is no doubt that vaccinia characterized by a single typical vesicle confers immunity against smallpox; it is impossible for multiple vesicles to do more. However, as a safeguard against failure when the danger of variolous infection is imminent, it is advisable in vaccinating to make more than one insertion.

The *age* at which it is proper to vaccinate a child is a matter of some importance. Unless some circumstance should arise requiring vaccination to be done earlier, it is advisable to defer the operation until the child is three months old. The most suitable age is from three to six months. It is not well to postpone the operation longer, else the systemic disturbances arising from teething may be added to the irritation from the vaccination, and thus increase the discomfort of the child. But where there is actual danger of exposure to the contagium of smallpox, dentition should not interfere with vaccination, nor should a newborn infant be considered too young to undergo the operation.

REVACCINATION.—Experience has demonstrated the fact that in a certain number of persons the protection from vaccinia in infancy is permanent, while in others it gradually diminishes, and after the lapse of a number of years frequently disappears entirely. This fact has been determined by noting the large number of persons in adolescent and adult life who are susceptible of revaccination; also by observing that in all epidemics of smallpox a large proportion of the cases occur among persons who were vaccinated in infantile life. The statistics of smallpox hospitals in this country and in England show that from 41 to 78 per cent. of the admissions are post-vaccinal cases. It is very difficult to determine the proportion of persons vaccinated in infancy that fail of permanent protection, but it is believed to be not far from 75 per cent. Some years ago a very careful observation in a certain American city showed that of 2362 persons revaccinated with reliable virus (no child under twelve years old with a good scar being included in this number), 77.1 per cent. were susceptible to some form of vaccinia.

We have no means of ascertaining the age or period of life at which the protection from vaccinia in infancy is liable to diminish or cease entirely, except by applying the test of revaccination or by noting at at primary vaccination any considerable number of persons rom smallpox. Data tending to demonstrate the latter may be in the f lowing table:

		Cases.	Deaths.	Percentage of deaths.
Under one year.	Unvaccinated	89	60	67.41
	Vaccinated	2		
One to seven years.	Unvaccinated	467	221	47.32
	Vaccinated in infancy—good scars	11		
	“ “ fair scars	10	1	10.
	“ “ poor scars	15	1	6.66
	Total number vaccinated	36	2	5.55
Seven to fourteen years.	Unvaccinated	242	72	29.75
	Vaccinated in infancy—good scars	55	2	3.63
	“ “ fair scars	23	2	8.69
	“ “ poor scars	59	9	15.25
	Total number vaccinated	137	13	9.48
Fourteen years and upward.	Unvaccinated	1111	693	62.37
	Vaccinated in infancy—good scars	1406	122	8.67
	“ “ fair scars	664	96	14.45
	“ “ poor scars	1027	286	27.84
	Total number vaccinated	3097	504	16.27

Among the 5321 cases of smallpox admitted to the Municipal Hospital of Philadelphia since the institution has been under the writer's care, now exactly twenty five years, only two vaccinated patients under one year old were admitted. One of these was a child eleven months old who had been vaccinated two months previously and showed a good scar. The eruption consisted of only six small vesicles, and the child's health was scarcely disturbed. The other patient had the disease so indistinctly marked that it was almost impossible to feel certain of the diagnosis of varioloid. An exceedingly modified form of smallpox was occasionally seen among well vaccinated children between the ages of one and seven years, but no deaths occurred except when there was a serious complication. The child that died, whose case is classified under the head of "fair scars," was a foundling about a year old, badly nourished and very feeble, with a disordered digestion. The eruption consisted of only a very few small vesicles. Death really resulted from inanition. Very little need be said of the cases classified in this age-period under the head of "poor scars," as the vaccination in them had been in good part either imperfect or spurious.

Between the ages of seven and fourteen years it is found that the post-vaccinal cases increased considerably, and occasionally death occurred, even when the infantile vaccination was quite thorough. At fourteen years of age, or the period of puberty, and thereafter, the protection is apt to diminish, and often disappears entirely. These facts lead to the conclusion that when there is danger of exposure to smallpox all vaccinated children who have reached the age of seven years should be revaccinated; also that revaccination should be practised systematically at the age of puberty whether smallpox be present or not. When the primary vaccination is not done until the child is seven or eight years old, the protection is more likely to be permanent; still, it is advisable to subject such children to the test of revaccination at the period of life just mentioned. The writer believes that it may be laid down as a rule that if a child be successfully vaccinated in infancy, and again at the age of puberty, the protection will be permanent. The exceptions to this rule, however, may be sufficient to warrant a repetition of the vaccination whenever there is great danger of variolous infection.

The question is often asked, What constitutes a successful revaccination? This is a question about which there is some diversity of opinion. Many believe that unless the vesicle and areola observe the course of true vaccinia the effect is merely local and devoid of prophylactic power. But it is evident on a little reflection that there is no more reason why we should expect the vaccine disease produced by revaccination to be typical than that we should expect smallpox after vaccination to run the typical course of variola vera. If there be modified smallpox or varioloid after vaccination, so should there be modified vaccinia or vaccinoid. From these premises the conclusion may be deduced that as varioloid confers immunity against a recurrence of smallpox, so also does the modified form of vaccinia resulting from revaccination remove from the individual whatever susceptibility to the disease may be present.

As to the value of revaccination there can be no question. Bousquet says very truly that there never has been an epidemic of smallpox since the general employment of Jenner's discovery which has not proved the virtues both of vaccination and revaccination. He adds: "The success of revaccination is at the same time the effect and proof of the wants of the system; . . . . when it succeeds, it not only proves that the protective power of vaccination is diminished, but it supplies a remedy for this diminution." Among the earliest and most conclusive proofs of the value of revaccination are the statistics furnished by the Würtemberg, Bavarian, and especially the Prussian armies. Of 14,284 revaccinated soldiers in Würtemberg, only 1 case of smallpox occurred in five years; and only 3 among 26,964 revaccinated civilians. During three severe epidemics in Copenhagen not a single case of varioloid occurred among persons who had been revaccinated. Also, during a very malignant epidemic which a number of years ago nearly decimated Liége it is said that none of those who underwent revaccination suffered from the disease.

Perhaps the most conclusive proof of all is that found in the statistics of smallpox hospitals. After an experience of thirty years in the hospital of London, Marson stated that but few patients were admitted during that time who had been revaccinated with effect, and that these suffered from varioloid in a very mild form. During this long service it was his custom to revaccinate all the nurses and servants who had not had smallpox on their coming to live at the hospital, and not one of these contracted the disease. At a time, however, when a large number of workmen were employed about the hospital most of them consented to be revaccinated, but there were a few that declined; of the latter two took smallpox, while of the former all escaped. During the writer's experience of twenty-five years no resident physician, nurse, nor any other employé of the Municipal Hospital of Philadelphia who had evaccinated before commencing duty has suffered from small- . Perhaps an exception should be made in the case of a female se who was revaccinated on the day of commencing work, and in n the vaccine disease was almost typical. In the course of about eeks one or two variolous vesicles appeared on her forehead near dge of her hair. Preceding this symptom there had been very febrile reaction for a day or two, but she was at no time incapaci- from performing her usual duties.

As the limits of this article will not permit of a more extended umé of the evidence in support of revaccination, the writer must nclude, believing that the testimony in its favor already adduced oo strong to admit of its neglect. In view of all the accumulated s in favor of vaccinal protection, it does not seem entirely visionary assume that if vaccination were efficiently performed in infancy and ystematically repeated at the age of puberty, if not earlier, Jenner's so alled dream—that vaccination is capable of extirpating smallpox from he earth—would verily become a realization. But whether this agent will ever be so universally and wisely employed as to confer on mankind its greatest possible benefit is doubtful.

VARICELLA.

BY WILLIAM M. WELCH, M. D.

SYNONYMS.—English, Chickenpox, Waterpock, or Glasspock; German, Wasserpocken, Windblättern, or Schafpocken; French, La Vérolette or Verricelle; Latin, Variola notha seu spuria; Italian, Ravaglione.

DEFINITION.—Varicella is a contagious eruptive disease, occurring chiefly in childhood, characterized by slight fever of short duration, and rapidly developing vesicles which begin to desiccate on the fourth or fifth day, leaving occasionally persistent scars.

HISTORY.—No clear or exact description of varicella appears to have been given by writers previously to the seventeenth century, although the disease was evidently known before that time. Rhazes described a mild eruptive affection resembling smallpox, but which gave no protection against that disease. This affection was doubtless varicella. The first accurate description of the eruption of varicella was given by Riverius in 1646. Still later in the same century Morton also called attention to the disease, and stated that it was vulgarly called chickenpox in England. But these and other authors of that period, while recognizing something peculiar about this affection, regarded it as an exceedingly mild form of smallpox. The credit of first calling attention to the fact that variola and varicella are different diseases, each resulting from a distinct contagium, belongs to Heberden of England. His classic paper on this subject was published in 1767 in the first volume of the *Transactions* of the Royal College of Physicians of London, and was long regarded as the standard work on varicella. Although Heberden believed in the specific nature of this malady, yet he called it *variolæ pusillæ*. The term varicella did not come into general use until after 1770, when universal attention was directed to the disease; but, strange to say, it was not until the early part of the present century that the individuality of varicella was generally recognized. In 1820, however, Thomson of Edinburgh, and still later Hebra, the celebrated professor of dermatology in the Vienna University, revived the exploded doctrine of its identity with smallpox. But notwithstanding the great weight of Hebra's authority and the persistency with which he advocated this doctrine, he has not succeeded in creating doubt in the minds of any considerable number of clinicians and authors. Nothing, indeed, is easier than to prove that his teaching in regard to the relation of these diseases is erroneous.

ETIOLOGY.—Varicella is a disease almost peculiar to early childhood. The vast majority of cases occur between the ages of one and ten years. Unlike measles and scarlet fever, but quite similar to variola, chicken-not infrequently attacks infants at the breast under six months of Some authors believe that the susceptibility to the disease diminis after the tenth year and ceases entirely after puberty. Thomas eipzig thinks that this may be the correct explanation of the very quent occurrence of the disease among older children and adults. says he never saw an adult suffer from varicella. There is no doubt, wever, that the disease is by no means uncommon among persons in ature life. This fact is amply attested by the experience of those who re connected with hospitals for infectious diseases. Attacks in adult would doubtless be far more frequent were it not that in the vast ority of persons the susceptibility is destroyed by the occurrence of disease in early childhood. The affection rarely if ever occurs more n once in the same individual. I believe I have never known a person to suffer from a second attack of varicella. Trousseau, however, says that second attacks are not uncommon.

Like all acute exanthemata, varicella at times appears sporadically, and then again it prevails in epidemic form. It is hardly ever entirely absent in large cities. The seasons do not influence its prevalence, except that the opening of kindergartens and schools in the fall of the year often marks the beginning of moderate epidemics. The epidemics never assume the proportion or intensity of those of variola and scarlet fever, but are frequently so mild as scarcely to attract the attention of physicians. While smallpox is often absent in a community for several years at a time, at least where vaccination is carefully and systematically performed, varicella is met with annually, especially in thickly populated districts. Unlike smallpox, its spread is not limited by vaccination.

The cause of varicella is a peculiar contagium. It must be admitted that nothing definite is known in regard to the nature of the specific virus, but there is no doubt that it owes its specificity to a micro-organism. The infecting agent enters the system doubtless through the respiratory tract. From what is known of variola, one would suppose that the infecting principle of varicella should be present in the vesicles, yet it is questionable whether the disease has ever been communicated by inoculation. While a very few positive results have been reported by Hesse and Steiner, negative results have followed the very careful attempts at inoculation by such men as Heim, Vetter, Czakert, Fleischmann, Thomas, and Boyce of Europe, and J. Lewis Smith of this country.

The period of incubation in varicella is perhaps more variable than in the other exanthemata. While it is often difficult to fix exactly the time when the contagium enters the system in any given case, yet it has been found that when the disease breaks out in a private family or an institution for children the time that elapses between the appearance of the eruption in the first and second cases is usually from thirteen to seventeen days. This may therefore be regarded as about the usual period of incubation, although a much shorter period has been reported by some observers.

It is evident from these considerations that there is a wide difference etiologically between varicella and variola—so wide, indeed, as to afford of itself conclusive proof that the diseases are essentially different. Most conclusive in favor of this opinion are the facts that varicella often prevails in communities where variola is absent; that the contagium of varicella never gives rise to variola in the unprotected, but always to a disease presenting the same characteristics as the original affection; that an attack of varicella confers no protection against smallpox, nor *vice versâ*; that varicella occurs with identical symptoms and equal facility among the vaccinated and unvaccinated; and that vaccination, however recent and thorough, does not destroy the susceptibility to varicella.

PATHOLOGICAL ANATOMY.—The only pathological condition present in varicella is that which results from the peculiar exanthem. The lesions appear on almost every part of the body, and consist of vesicles varying in size from that of a millet seed to a silver dime. They develop rapidly upon hyperæmic spots, which are but slightly if at all infiltrated. The deeper layers of the derm are usually not involved, differing in this respect from the lesions of variola. The vesicles begin to form in the centres of the hyperæmic spots and grow by peripheral extension until their full size is attained. They are usually surrounded by an areola which is frequently quite broad. It is rare that the initial hyperæmia is present longer than a few hours before the vesicles begin to form.

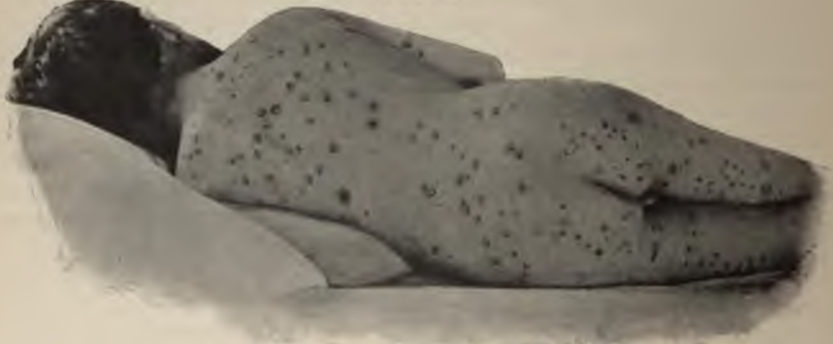
Undoubtedly the lesions are exudative in character. As the exudation of serum takes place in these morbid areas the superficial epidermic layer is raised from the deeper layers of the derm, and thus a distinct vesicle is formed. Varicella not being a fatal disease, opportunities for carefully investigating the anatomical structure of the vesicle, as displayed in sections, do not occur. There is reason to believe, however, that the vesicle is not originally a single cell, but contains delicate septa dividing it into compartments. These septa or partition walls not infrequently give way at an early stage of the exudative process, permitting the contents of the vesicle to run partly or wholly together. Owing, doubtless, to the superficial character of the vesicles and the rapidity and profuseness of the exudation, the umbilication so common in variola never occurs.

The vesicles at first contain a serous fluid as clear as water. Later, owing to the slight admixture of pus cells, this fluid assumes an opalescent or whey-like appearance. In those vesicles which run a more protracted course the proportion of pus cells is greater, but not so great as in the pustules of variola. The contents are usually slightly alkaline in reaction. The duration of the vast majority of the vesicles is brief. Either from partial absorption of their contents or some mechanical cause, such as rubbing or scratching, the vesicles collapse, and desiccation begins when the process has not continued longer than two or three days. In the undisturbed vesicles desiccation usually commences in their centres, giving rise to a depression that is sometimes mistaken for umbilication. In the milder cases the scabs, which are small, fall off quickly, and are not followed by scars. But when the course of the vesicles is prolonged there is sometimes destruction of the lower layers of the derm, and permanent scars result. The number of scars from an attack of varicella, however, is never very large. The mucous membrane of the mouth and fauces suffers only very moderately from the eruptive process.

Symptoms.—The stage of incubation of varicella is seldom attended by symptoms. In the majority of cases the first symptom noticed is the appearance of the vesicles. This is not only the testimony of careful and observing mothers, but has been confirmed by medical observation in institutions where opportunities have been afforded to witness outbreaks of the disease. Occasionally, however, there may be seen a short initial or precursory stage of not more than a few hours' duration; but even in such cases the febrile reaction is usually insignificant, as the temperature is not apt to rise higher than one or two degrees above the normal point. Exceptional cases sometimes occur among children in whom the onset of the disease is marked by slight rigors, considerable elevation of temperature, moderate headache, and vomiting. I have reason to believe from my experience that such a precursory stage is not uncommon in adults.

If a case of varicella be carefully examined at the very earliest stage of the eruption, the skin lesions will be found to consist of small roseolar spots. According to some writers, these spots appear first on the hairy scalp, face, and neck, but not infrequently they may be seen quite as early, or even earlier, on the trunk and extremities. A very favorite locality is the back. They are of the nature of maculæ rather than papulæ, and hence do not convey to the sense of touch the feeling of denseness or firmness, as do the papulæ of variola. In the course of a very few hours distinct vesicles appear in the centres of these reddish puncta or rose-colored spots. These vesicles at first contain perfectly clear serum, and do not look unlike small blisters resulting from a moderate sprinkling of the skin with boiling water.

Fig. 48.



Varicella on the fifth day of eruption.

While the contents of the vesicles at first is perfectly clear or transparent, it very soon assumes a turbid or milky appearance from the admixture of pus cells; but it never becomes so distinctly purulent as in variola. The vesicles vary very greatly in size. The average size is that of a split pea, though some of them become as large as a silver dime, or even much larger, while others remain as small as lentil seed. They do not all appear at once, but come out in successive crops. That is to say, soon after the first vesicles have appeared there may be seen on the skin faint red points which rapidly develop into vesicles, and so, again, roseola and vesicles appear between these lesions. Many of the vesicles have but a brief existence, and it is therefore not unusual to find them in every possible stage of development. For example, when the eruption has fully appeared some of the older vesicles may be seen in a state of desiccation, while others have collapsed and are drying, and still others remain distended by sero-purulent fluid.

The vesicles are either acuminate or globular in form. They never assume that peculiar form of umbilication which is so characteristic of the eruption of variola. It is true when the vesicles are fully developed very many have a depression in their centres, but this depression is the result of commencing desiccation, rather than that their epidermic covering is held down by sweat glands or their follicles, as in variola.

The vesicles, as already stated, usually run a very rapid course. Within a day or two after they are first seen many of the vesicles will be found to have grown flaccid, either from partial absorption of their contents or rupture of their epidermic covering, and when in this condition they speedily dry up and disappear, sometimes without the formation of scabs. In those which do not disappear in this way desiccation begins usually in their centres. Even when desiccation has thus begun it is not unusual for several of the vesicles to continue to enlarge by peripheral extension until they attain the circumference of a silver dime, and, in some cases, that of a silver quarter dollar. These larger vesicles usually reach their utmost limit of development within a period of four or five days, then begin to fade, but the scabs which form are often so firmly attached that they do not fall off spontaneously before the end of the second week. After the scabs have fallen there commonly remains upon the site of the vesicles slight pigmentation of the skin, but this, in most cases, gradually fades away without leaving permanent scars. It is only in those vesicles which run a protracted course and are accompanied by ulcerative action that scar formation results. Therefore, when scars result at all they are few and scattered; never do they follow so large a proportion of the vesicles of varicella as they do pustules of variola.

The mucous membrane is only very moderately attacked in varicella. Small and ill-defined vesicles may be seen on the soft and hard palate, the tongue, the mucous membrane of the buccal cavity and of the nares. When they occur in these parts they are always sparse, and rarely extend to the larynx and trachea. They sometimes appear on the mucous membrane of the external genitalia of girls or on the prepuce of boys, and make urination painful. I have never known the vesicles to appear on the conjunctiva; occasionally, however, they may be seen on the margin of the eyelids and slightly affect the conjunctiva at its continuity with the skin.

Complications.—Complications rarely occur, and sequelæ are quite unknown. A peculiar form of gangrene of the skin has been met with, especially in Ireland. Dr. Whitley Stokes of Dublin described this affection in 1807, and applied to it the name *pemphigus gangrænosus*. It has also been described by various other writers as *dermatitis gangrænosa*. More recently (in 1881) Mr. Jonathan Hutchinson called attention to this dangerous, though fortunately rare, complication, and proposed for it the name *varicella gangrænosa*. It is not imble that this malady is met with only in children having a ency to the development of so called spontaneous gangrene. It id to occur more frequently among weakly and ill nourished ren, though it is not confined to them. A very clear descrip- the disease has been given by Dr. Eustace Smith. He says:[1] gangrenous varicella the vesicles, instead of drying up in the ary way, become black and get larger, so that a number of ded black scabs, with a diameter of half an inch to an inch, are ered over the surface of the body. If a scab be removed, it is seen ver a deep ulcer. Around it the skin is of a dusky red color. All esicles do not take on the gangrenous action, so that we find many cellous scabs of ordinary appearance mixed up with the blackened ts. The gangrenous process often penetrates deeply through the to the muscles, but under some of the scabs the ulceration is more allow. These cases are very fatal. Mr. Warrington Haward has ported the case of a weakly baby twelve months old who weighed only six pounds and a half. The child was attacked with gangrenous varicella and died in a few days of pyæmia, with secondary abscesses in the lungs." Cases have also been reported in which gangrene attacked the scrotum, and proved almost as destructive to that tissue and as fatal to the patient as when the same complication occurs in variola.

Diagnosis.—Eczema pustulosum and impetigo contagiosa have been thought by some to resemble varicella, but the points of resemblance are so slight as rarely to introduce into the question of diagnosis an element of confusion. The only disease with which varicella is liable to be confounded is smallpox in some of its varieties.

There is usually no difficulty in differentiating between variola vera and varicella, but between the latter disease and certain forms of varioloid the difficulty is often very great and mistakes are not uncommon. The teaching of most authors that varicella is a disease peculiar to childhood is, I think, responsible for many errors of diagnosis, inasmuch as it tends to create a belief that in adults eruptions resembling varicella always indicate smallpox. It should be borne in mind that the former disease is by no means infrequent in adolescence or in adult life.

It will often prove helpful to know whether or not the patient has ever been vaccinated. When a vesicular eruption suddenly appears in a child who has recently been successfully vaccinated, variola can be excluded from the question of diagnosis with a considerable degree of certainty. So also variola can be reasonably excluded when such an eruption appears in an unvaccinated child without having been preceded by severe constitutional symptoms, such as are peculiar to the initial stage of that disease. In children, however, older than ten years, and also in adults who have been vaccinated in infancy, the variolous eruption is often so greatly modified as to bear considerable resemblance to the lesions of varicella. It is this class of cases, in which the eruption shows no distinct characteristics, that not unfrequently taxes to the utmost the skill of the diagnostician. Although difficult, it is important that a correct diagnosis should be made, since in the one case the contagium generated is usually innocent, while in the other it is frequently disastrous in its results. When, however, a history of exposure to either of these contagia can be obtained, the diagnosis becomes, of course, comparatively easy.

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[1] Eustace Smith, *Diseases of Children*, 1884, p. 49.

In differentiating between variola and varicella it is very important to note the behavior of the fever. In the former the temperature suddenly rises, after a decided chill or repeated rigors, to a considerable elevation. It not infrequently rises during the first twenty-four hours of the illness to 105° F., and continues high four or five days or until the eruption has fully appeared. In varicella the temperature rarely or never rises so high, and no elevation is usually noticed at all until the vesicles have appeared. Even in modified smallpox or varioloid the temperature is apt to be high at first, and this symptom almost always precedes the eruption from two to four days. There is no secondary or suppurative fever in varicella, as in variola. It is true that in mild cases of varioloid, which variety of smallpox varicella more closely resembles, there is likewise no secondary rise of temperature; hence other points of differentiation must be considered in such cases.

It frequently happens in smallpox, especially in the modified forms of the disease, as well as in varicella, that no reliable history of initial fever can be obtained, so that in very many cases the diagnosis must be made from the appearance of the exanthem alone. It is therefore important to bear in mind that the exanthem of varicella appears at first in the form of distinct vesicles containing clear serum; that they are usually seen first in greatest number on portions of the body covered by clothing, especially on the back; that they make their appearance in successive crops, and vary very greatly in size; that their epidermic covering is delicate, and can be easily broken by the finger nail; that many of them enlarge by peripheral extension, while desiccation is seen in their centres, causing a central depression; that they run their course in two to four days, and form thin, brown scabs; and that but few of them are followed by permanent scars. On the other hand, the exanthem of smallpox first appears in the form of papulæ, which are slowly transformed into vesicles, and then into pustules; the papulæ are dense and hard, and, to the sense of touch, seem like grains of sand buried in the cutis; the eruption prefers the exposed surface of the body, such as the face, arms, and hands, being often only sparsely seen on the trunk; the lesions usually begin on the face and are slow in spreading over the body, but they never come out in successive crops; the vesicles are dense and firm, especially on the exposed surface of the skin, and cannot be readily obliterated by the finger nail; they do not vary so greatly in size as in varicella; they are umbilicated by their epidermic covering being slightly drawn inward, rather than by desiccation commencing in their centres; the exanthem requires from six to twelve days to pass through its various stages, and ends by the formation of comparatively thick, dark crusts: and most of the lesions, especially those on the face and hands, are followed by permanent scars.

While the symptoms just enumerated are peculiar, respectively, to chickenpox and smallpox, and while there should be no difficulty in diagnosticating any case in which either series of symptoms is complete, yet it must be admitted that there are intermediate cases in which the symptoms are so atypical that they cannot be readily assigned to either

ategory. It may, however, be said, in a general way, that a mildly
ebrile exanthem appearing without prodromal symptoms, being dis-
inctly vesicular from the beginning, and commencing to desiccate on the
cond or third day, should be regarded as varicellous ; and, on the other
nd, an acute exanthem preceded by an initial stage in which the tem-
rature was high, beginning as papules and ending in vesicles or vesico-
stules, even though the period of evolution be short, should be re-
rded as variolous. At any rate, it would be wise, for the safety of
he public, to regard such a case as suspicious. If it should happen in
a case in which the diagnosis cannot be clearly determined, that vaccination had never been performed, it would be well to apply this test, for it is well known that variola renders an individual immune to vaccinia, and that varicella does not.

PROGNOSIS.—The prognosis in varicella, even in infantile life, is uniformly favorable. The disease frequently runs so mild a course that the family physician is not summoned, or perhaps he may be called to decide as to the character of the eruption rather than to prescribe for the patient. Varicella, *per se*, never proves fatal. Some concurrent affection might arise to threaten the life of the patient, but no complication is especially liable to occur. It is true, gangrene of certain parts of the cutaneous integument has been met with as a result of the varicellous process, but this is apt to occur only in children with some peculiar tendency to gangrene. The appearance of such a complication would naturally be viewed with deep concern.

TREATMENT.—As recovery invariably results from varicella, but very little is required in the way of treatment. The patient should be confined to the house, and even to the bed, for a few days, or until the fever subsides and the eruption has completed its course. The adoption of proper hygienic measures, such as regulating the temperature of the room, providing the patient with suitable diet, and giving attention to bathing, is usually all that is required. A mild diaphoretic or febrifuge mixture may be given, and also bromide of potassium if the child be restless and sleepless. If there be much itching or irritation of the skin, cocoa butter or an antiseptic unguent may be applied locally. It is advisable to prevent rubbing or scratching of the vesicles, especially those on the face, as such injury increases the liability to pitting. The disease being quite innocent, it is usually unnecessary to adopt any special measures to prevent its spreading. When the patient has recovered it would be well to subject the bedchamber to the ordinary process of housecleaning.

SCARLET FEVER.[1]

BY P. GERVAIS ROBINSON, M.D.

SYNONYMS.—Scarlatina; Scarlet rash; Scharlach (German); Scarlatine (French).

DEFINITION.—Scarlet fever is an acute, highly infectious disease, due, we may fairly believe, to the presence in the body of a specific organism. Though the malady presents, in its clinical manifestations, more variations than any other exanthem, there are certain symptoms which are so frequently present as to be characteristic: there is a punctiform scarlet rash upon the skin which terminates in a lamellar desquamation; an angina which is usually well marked; a fever of varying degree; and a noticeable immunity from future attacks.

ETIOLOGY.—Scarlet fever, like other diseases of its class, has ever followed in the path of commerce. It seems to have been first introduced into this country in 1735. From the coast it crept inland until all the inhabited portions of the land were affected. It is curious to note that scarlatina when introduced into a virgin soil does not seem to possess the same virulence which is displayed by measles and smallpox under similar conditions. The writers who first described the disease in the United States regarded it as a mild affection. In this country, as in all other portions of the civilized world, scarlet fever has now become endemic in the large cities; from these as foci from time to time epidemics arise.

Periodicity.—Many facts have been adduced to show that epidemics of scarlatina observe periodicity, but so many exceptions to such a law can be cited that it may be doubted if it in reality exists.

Peculiarities of Epidemics.—No contagious disease varies so widely in the severity of the various epidemics as scarlet fever. Willan speaks of epidemics differing as much as "a fleabite and the plague." Sydenham thought scarlatina so mild an affection that it hardly deserved the name of a disease. Two years later Morton found the same epidemic exceedingly severe. In the epidemic of 1863 in London one fourteenth of the entire death rate was due to scarlet fever. In Stuttgart in an epidemic which occurred in 1846 not one death was reported. Copland, writing in 1858, said: "There is no kind of fever which displays a greater diversity in its nature and complications," and the experience of all observers will bear out this statement.

Season.—Although scarlet fever is present in large cities at all seasons of the year, it is generally most prevalent in the autumn and winter.

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[1] In the preparation of this article the writer begs to express his obligations to Dr. C. F. Hersman for valuable assistance.

low is presented a table showing the number of cases and deaths e city of St. Louis for the past four years:

For Municipal Year ending March 31, 1890.

	Cases.	Deaths.		Cases.	Deaths.
	69	8	October	258	21
	97	9	November	253	15
	102	11	December	237	18
	81	3	January	171	10
	144	10	February	141	3
ber.	172	4	March	157	8
Total				1882	120

	Year of 1891: Cases.		Year of 1892:	ths.	Year of 1893: Cases.	Year of 1893: Deaths.	Year of 1894: Cases.	Year of 1894: Deaths.
	103			8	60	5	84	8
	142	9		6	65	13	75	9
	115	12	59	3	86	12	41	5
July	82	6	44	2	50	13	19	3
August	114	4	66	6	60	9	45	2
September	114	8	71	5	108	5	61	2
October	99	6	74	7	156	22	65	2
November	119	5	83	15	128	13	64	6
December	135	7	139	16	109	24	75	7
January	125	16	94	12	91	25	87	8
February	99	4	113	23	66	8	57	2
March	89	8	63	6	77	4	56	1
Total	1336	94	948	109	1056	153	731	55

A reference to this table shows that, though scarlet fever has been distributed throughout the seasons of the year with more uniformity than has often been observed elsewhere, yet the preponderancy of cases in autumn and winter is preserved. Many writers have attempted to show that this seasonal prevalence is dependent on the temperature, moisture, electrical conditions, amount of ozone present, etc., but the proofs of such relations at present rest on the vaguest grounds. It may be that when the cause of scarlatina is better known something in its life history will explain this fact. In the mean time, certain factors may be cited as partial explanation. In the autumn and winter, in our climate, the surface of the body is exposed to frequent chillings, among the poor often for long periods, and with them sufficient food is more difficult to obtain at these seasons than at other times of the year. Fodor has found that some bacteria introduced into animals reduced by hunger and cold are more apt to thrive than when inoculated upon the same animals in good condition. Furthermore, in the autumn and winter lesions of the respiratory mucous membrane are especially frequent, and it is probable that the poison of scarlatina usually enters the body by inhalation Then at this time of the year there are more opportunities for personal contact among children, especially by confinement in schools with large numbers of other children. Hershey[1] states that 70 per cent. of scarlet fever cases come from infection at school.

As might be expected, scarlet fever generally shows the highest mortality in those years when the most widespread epidemics are present, and at those seasons of the year when cases are most numerous. But here, again, the disease shows a wonderful variability. It not uncommonly happens that during an extensive epidemic the relative mortality is less than in ordinary years, and, as Hebra has shown, it will often happen that the malady is as intense at one season as at another. This may be illustrated from the table of the mortality of scarlet fever in St. Louis, given above. In 1890 there was the greatest number of cases, with a mortality of 6.3 per cent., while in 1894 there was a small number of cases, with a mortality of 7.5 per cent.

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[1] *Medical News*, April 22, 1894.

Age.—Scarlet fever is essentially a disease of childhood. Though no age is exempt, the majority of cases occur in the first ten years of life. After this the liability to contract the disease decreases rapidly with each succeeding decade. The liability to attack is at its height in the fifth year. The report[1] of the Registrar General of England for 1886 contains so much of value in this connection that it is here reproduced. The report is based upon nearly half a million deaths from scarlatina occurring in England and Wales from 1859 to 1885; on 17,795 cases admitted during 1874–85 into the London Fever Hospital and the Metropolitan Asylum hospitals at Stockwell and Hammerton; on 5000 in Christiania from 1870–82; and on the returns of all known cases of scarlet fever for some large towns in England where notification of infectious diseases has been for some time compulsory. The conclusions drawn from a study of this vast material are—

(1) The mortality is at its maximum in the third year of life, and after this diminishes with age—at first slowly, afterward rapidly.

(2) This diminution is due to three contributory causes: (*a*) the increased proportion in the population at each successive age-period of persons protected by a previous attack; (*b*) the diminution of liability to infection in successive age-periods of those who are as yet unprotected; (*c*) the diminishing risk in each successive age-period of an attack, should it occur, proving fatal.

(3) The liability of the unprotected to infection is small in the first year of life, increases to a maximum in the fifth year or soon after, and then becomes rapidly smaller with advance of years.

(4) The chance that an attack will terminate fatally is highest in infancy, and diminishes rapidly with years to the end of the twenty-fifth year, after which an attack is again somewhat more dangerous.

(5) The female sex throughout life, the first year possibly excepted, is more liable to scarlatina than is the male sex.

(6) The attacks in males, though fewer, are more likely to terminate fatally.

(7) Hence the longer an attack is deferred the less likely is it to occur at all and the less likely is it to end fatally.

It is no doubt true that the exemption of the first year of life from attack is more apparent than real: the child at the breast is more protected from exposure than those old enough to run about and mingle with other children. The author has observed in his own family a severe case in a child nine months of age, followed by general dropsy. That advance in years does really bring immunity Murchison tries to prove by stating that if the mortality in England and Wales is calculated per cent., then the number of cases of scarlet fever in these ies is less than one half the births, so that a large number reach fe who have not been protected by an attack in childhood.

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[1] *A Contribution to the Natural History of Scarlet Fever*, Gresswell, p. 172.

genital Scarlatina.—Several cases have been reported of congenital fever. On the other hand, Murchison has observed two healthy n born from mothers suffering with scarlet fever. Although it always be difficult to determine the presence of the rash of scarlet in newborn babies, whose skins are already red and often des-ate soon after birth, still, as many authenticated cases are on d in which similar diseases have been present at birth, we may ve that it is possible for children to be born with scarlatina. Nor ne observations of authors that sometimes children unaffected are of affected moth[illegible]es the disease is transmitted to fœtus, insusceptibl [illegible]tion. Normally, the placenta acts s a filter, keeping back from [illegible] fœtus formed elements from the maternal circulation. Bacteria are thus generally not allowed to pass into the fœtal circulation, but under some circumstances, as has recently been shown, through a pathological condition in the placenta disease germs may pass to the fœtus. It has been observed that a babe while suckled by a mother affected with scarlet fever has escaped the disease. It is possible that this phenomenon has relation to certain recent observations which go to show that the milk of animals attacked by certain infectious diseases may acquire an antitoxic property.

Sex.—The statistics gathered by the Registrar General of England, quoted above, show that the female sex is more liable to scarlatina than the male, but such figures are often misleading. Indeed, most authorities are agreed that sex in itself exerts no influence on predisposition. Richardson[1] has expressed his opinion thus: "Male and female are alike susceptible if they are alike exposed."

Race.—It is not possible, on account of the confusion which exists in nomenclature and the inadequate returns from many countries in regard to scarlet fever, to determine what effect race has upon predisposition and upon the severity of the disease. According to D'Alves,[2] scarlet fever attacked the Brazilian Indians with great intensity. Murchison states that scarlet fever makes no distinction among the different races living in New Zealand. It has been stated that scarlatina does not occur among the Japanese. Ashmead[3] has reported a case occurring in a Japanese living in Brooklyn. The writer is of the opinion, judging from his own experience, that scarlatina is less common among negroes than among whites, but it is difficult to decide this point on account of the uncertainty of the diagnosis in negroes, and because they are not under such thorough medical control as are the whites.

Social Position.—Though social position exerts no influence on susceptibility to scarlet fever, it influences decidedly the severity of the affection, the mortality being less among the rich than among the poor. This can be explained on the ground of better attention, food, and hygiene in the case of the well to do.

Locality.—It has never been proven that residence in cities or in the country, the nature of the soil, or the altitude have any influence upon predisposition.

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[1] *Natural History of Scarlatina*, Gresswell, p. 175.

[2] *Cyclopedia of the Practice of Medicine*, Von Ziemssen, vol. ii. p. 185.

[3] *New York Medical Journal*, Jan. 10, 1894.

Influence of Previous Health.—The previous state of health is of doubtful influence upon predisposition to scarlet fever, though it would seem but reasonable that those whose physiological resistance has been diminished should fall a more ready prey. Loeschner and Koestlin state that scarlatina very often follows in the wake of measles. It is probable that a weakened condition of the general health from other diseases predisposes to scarlet fever. Thus, Ehler[1] states that in Iceland in 1779 the majority of the lepers perished during a scarlet fever epidemic.

Occupation.—Occupation has no effect upon predisposition. Certain callings are attended by more abundant opportunities for infection than others. Murchison states that almost one third of all the patients received into the London Fever Hospital are nurses and servants from families where scarlatina is prevailing.

Susceptibility in General.—The susceptibility to scarlet fever is much less universal than to measles or smallpox. It not uncommonly happens that only one child of a family will develop the disease, though all have been equally exposed. It has been noticed that where one of two towns between which there is constant intercourse has been attacked the other has escaped for a long time. A person may live immune in an affected neighborhood, and on removing to a distant place may develop susceptibility under no more favorable circumstances for infection than those by which he was previously surrounded. Unlike measles, scarlet fever on entering a community for a long time exempt does not attack all those not already protected; the same vagaries of susceptibility are noted here as under other circumstances. It has been observed that the longer an epidemic lasts the more likely are those who at first escaped to yield to the attacks of the disease. The variations in the intensity of scarlatina are as unaccountable as are the irregularities in susceptibility. Two children in the same family may contract the disease from presumably the same source; one may have scarlatina in its mildest form, while the other perishes under a malignant attack. It is a fact worthy of notice that in some families a special susceptibility to scarlet fever is manifested. Instead of one or two children being attacked, the whole family is rapidly affected. Under such circumstances the disease may assume so severe a form that many of the cases terminate fatally. The writer is acquainted with a family in which out of 12 cases occurring in a week 7 died.

Pregnancy, Puerperal State, Wounds.—Many authors hold that pregnancy increases the liability of women to scarlet fever. On the other hand, observers of wide experience (Trousseau) have seen no pregnant woman attacked during extensive epidemics. The belief has long been held that women in the puerperal state are especially liable to scarlatina. It is but fair to conclude that in their exhausted condition such women would be more readily attacked by any infectious disease; but it must not be forgotten that the statistics brought forward to prove this increased susceptibility to scarlatina are largely from hospitals, where, especially in former days, the virus of scarlet fever always existed, so that it was often more a question of exposing a large number of lying-in women to infection than of susceptibility being increased by childbed. Another source of error lies in the great similarity of certain septicæmic rashes which may attend the puerperium to scarlet fever.

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[1] *The Medical Week*, Nov. 30, 1894.

It used to be quite common, after surgical operations, to see a scarlatiniform rash develop. In some of the English hospitals this has occurred with such frequency as to necessitate the closure of the wards for a time. When we consider how tenacious of life is the virus of scarlet fever, and how inadequate in former years was the disinfection of instruments and dressings, we can readily believe that some of these cases were real scarlet fever. No doubt most such cases have been rashes accompanying septic infection. Hutchinson[1] reports a case of a woman who on the fifth day after an amputation died of what seemed to be real scarlet fever. No case of scarlatina had occurred recently in the hospital, but on inquiry it was found that the disease had been in the woman's family several months before. Hutchinson thinks that in this case the germs of the malady were present in the woman when admitted, and were aroused to activity by the disturbance following the operation.

The Contagium.—Today no one doubts the infectious nature of scarlet fever, though not many years ago there were those who argued against this idea. The virus is of so volatile a nature that merely coming for a moment into the presence of one affected with the disease suffices to reproduce it in a susceptible person. Not only is the malady immediately infectious, but the contagium may be conveyed by fomites. These fomites may consist of the human or other animal body, of food, of letters or papers or books, of merchandise—in fine, of almost any article that may pass from person to person in the exigencies of daily life. Palante notes the case of a woman who, after remaining only a moment in the room of a scarlatinous patient, returned home, a distance of six miles, and gave the disease to her children. Several cases are on record in which a domestic animal occupying the room of a patient has conveyed the disease. Hamilton[2] mentions that during an outbreak of scarlet fever in Dublin two children who were ill were isolated in the top of a house and every precaution taken to prevent the spread of the malady to healthy members of the family. After a fortnight other children, who had been kept in the basement, took the disease, and it was found that a cat, which had been in the habit of spending the day with the sick children and the night with the well, had conveyed the contagium. A letter written in the room of a scarlet fever patient has often conveyed sickness and death to distant homes. Books in libraries for circulation among the poor are frequently used to relieve the tedium of recovery from scarlatina and become ready carriers of the disease. Time and again milk stored in the chamber of a person ill of scarlet fever has initiated an epidemic of the disease. The tenacity of the virus is great, and it has often happened that it has been revived after lying dormant for long periods. Von Hildenbrand's classical coat retained its contagiousness for a year and a half. Duffin[3] records an instance where the paper had been left on the walls after a case of scarlet fever had occurred in a room. New paper was put on several times without removing the old. Finally, a new family came and took down all these layers of paper, liberating the scarlet fever poison and causing an outbreak in the family. An almost indefinite number of instances illustrating the longevity of this poison might be collected from the literature were it important or necessary to produce further examples.

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[1] *Archives of Surgery*, April, 1893.

[2] *British Medical Journal*, June 3, 1894.

[3] *The Clinical Journal*, April 5, 1894.

Mode of Communication.—It is usually considered that the virus enters the body through the respiratory mucous membranes. The fact that the stress so often falls upon the pharynx early in the disease might be looked upon as pointing in this direction. Kaposi states that children with chronic tonsillitis are more prone to the malady, and this gives additional support to the idea that the respiratory tract generally affords the site of entrance. Some have supposed that the virus enters with the food or drink. That it may at times gain entrance in other ways is proved by inoculation experiments. The disease has been produced by inoculation with blood, epidermic scales, serum from vesicles, and nasal and pharyngeal secretions. Miquel[1] claimed to be able to produce a local reaction comparable to vaccination by the inoculation of serum from vesicles, the subjects of this treatment being then found to be refractory to scarlet fever. But, as a rule, the disease when produced by inoculation has been more severe than that arising spontaneously, so that it has not to the present time been possible to use this method to procure immunity.

Immunity.—As in other exanthems, so in scarlet fever, one attack confers immunity from future attacks. Whatever the scientific explanation of this immunity may ultimately prove to be, it certainly involves some profound change in the system, for it usually persists throughout life. There are exceptions to this rule: a few well authenticated instances of repeated attacks are on record. In the popular estimation repeated attacks are more numerous than they can be shown to be in fact—this largely on account of errors in diagnosis. Thus, a child has German measles or some erythema and the attending physician pronounces it scarlet fever: when the child really develops scarlatina it is regarded as a second attack. Many writers of wide experience have never seen an undoubted instance of a second attack. It has often been noticed that during an epidemic of scarlet fever many persons, both those who have had the disease and those not so protected, suffer from angina, which has frequently been regarded as scarlatinous. Because this sore throat occurs at the same time as scarlatina does not show that it is the result of the germ of that disease. Indeed, it has been shown that the severe forms of throat trouble which often manifest themselves in scarlatinous patients are the result of secondary infection. These anginas are undoubtedly contagious, and thus a great number of the sore throats seen during an epidemic of scarlet fever may be entirely independent of that disease. Such instances, then, cannot be admitted as constituting second attacks of scarlatina. In some cases which are characterized by an unusually prolonged febrile stage, in the second or third week an erythema again appears upon the body: to such cases Thomas gives the name "pseudo-relapses." In other instances after convalescence is begun a rash accompanied by other morbid symptoms condition Thomas applies the term "relapse." Some s have thought that repeated attacks of scarlet fever constituted peculiarity. Troganowsky[1] found that in two of his cases of tacks both parents had experienced the disease twice. Mur- as observed relapses in two sisters. It is said that relapses and ttacks are generally mild in character.

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[1] *Maladies de la Peau,* Kaposi, p. 267.

of Greatest Infectiousness and Length of the Period of Infec-—At which period of its evolution scarlet fever is most contagious estion which has never been definitely decided. It would seem le that the virus was being liberated in greatest quantity when ease was at its height. This is not so important a question, how- as is the inquiry, Is scarlet fever contagious at all periods of the e, and if so how long does the contagiousness last? The answer first part of this [illegible] d more difficult by the vary- usceptibility to the [illegible] great tenacity of the virus. child in the period [illegible] is brought into contact with other child, and the second [illegible] to contract the disease, this will ot show that scarlet fever is not con[illegible]us in the period of incubation, nce the exposed individual may hav[illegible]een one of those not decidedly susceptible. Again, if the disease occurs in one child in a family who is at once isolated and kept so till all signs of sickness have disappeared, and if when this child joins the others another case appears, this does not prove that the original case was liberating the poison at the time of his restoration to the family circle, for we know how readily objects about a patient at the height of the disease may be infected and how difficult it is to remove from them the contagium. Reasoning from what has been shown to be true in smallpox and measles, it seems likely that in the period of incubation, before any active signs of illness are present, scarlatina is infectious. How long the possibility of infection endures has not been exactly determined. It is indeed probable that this period may vary in different cases. We would certainly not overstep the line were we to say that as long as any morbid phenomena attributable to the attack of scarlatina exist there is a possibility of infection. In fact, it is likely that such a statement does not cover the whole truth, for in some cases of diphtheria[2] it has been shown that Löffler's bacillus can be demonstrated long after all clinical evidence of disease has ceased, and what is true for this malady may very well hold for other infectious diseases, scarlet fever among the rest.

Incubation.—The incubation period of scarlatina, as usually stated, varies within wider limits than are assigned to the same stage in the other exanthems. Formerly the incubation was estimated at from one to eight

	Usual time.	Minimum time.	Maximum time.
Committee of the Clinical Soc., 1892	2 or 3 days.	1 day.	7 days.
Bristowe, 1887	6 to 8 days.	Often less.	Occasionally longer.
Guinon, 1892	4 or 5 days.		
Strümpell, 1887	....	Less than 4 days.	7 days.

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[1] *Cyclopedia of the Practice of Medicine*, Von Ziemssen, vol. ii. p. 189.

[2] *Medical News*, Nov. 10, 1894.

days. Recent observations, however, seem to show that the period of incubation is marked by narrower limits. Williams[1] in a report for the Clinical Society of London tabulates the foregoing opinions as to the length of the stage of incubation in scarlatina. (See table, page 584.)

Hamilton[2] from an experience of a severe epidemic among troops claims that the period of incubation of scarlet fever is three or four days. In some inoculation experiments the time of incubation has been seven days. Gerhardt is authority for the statement that, an abscess having been opened with a knife that had been used on a scarlatinous patient, scarlatina was developed four days later. Bokai[3] reports two cases of tracheotomy in which scarlet fever developed sixteen hours after exposure. Soerensen[4] states that in 10 cases operated upon by Paget in which scarlet fever developed the period of incubation was one day in 2 cases, two days in 3, and three days in 3 cases. The same author remarks that in 9 out of 12 cases of puerperal scarlet fever the period of incubation was three days. It would seem probable from these figures that where infection occurs through a wound the time of incubation is shortened.

On the other hand, it may happen that the incubation period is prolonged. Kaposi states that in rhachitis and other conditions of ill health a prolonged incubation not uncommonly occurs. Instances have been reported in which the time of incubation was several weeks. In some of these instances, where a case occurs in a family and a second case does not develop for weeks after the first, it is not necessary to assume that the incubation is thus lengthened, but rather that the poison did not, for some reason, affect the person at the first exposure. Besides, it is often difficult or impossible to exclude opportunities for infection other than the one from which the long incubation has been counted. Still, since there is a possibility that these long periods of incubation do occur, a physician would be wise not to pronounce a child entirely out of danger till several weeks have passed since exposure.

Occurrence with Other Exanthems.—It is quite well established that other acute exanthems may occur at the same time as scarlet fever. Hirschprung narrates 2 cases, in each of which scarlatina and varicella were both present. Wolberg reports the case of a boy who was first attacked by scarlet fever; a few days later the temperature rose and a crop of variola vesicles appeared. Hardaway has seen scarlet fever develop in the period of crusting in a case of variola. Brand has noticed the concurrence of scarlatina and typhoid fever. Taylor has seen 2 cases in which measles, scarlet fever, and diphtheria occurred simultaneously. Many other such instances might be gathered, but these will serve to illustrate this relation of scarlatina.

Micro-organisms in Scarlatina.—Though many claims have been made to the discovery of the micro-organism which is the active factor in the production of scarlatina, no one of these has as yet received sufficient confirmation to merit its acceptance. In 1882, Ecklund described certain colorless corpuscles which he had found in the urine of scarlet fever patients. Similar bodies were found in the soil and surface water of regions in which epidemics of scarlatina were prevailing. Others have verified this observation as far as the appearance of the bodies in the urine is concerned, but their relation to scarlet fever has not been determined. Klein has obtained from the blood and tissues of scarlatinous patients a streptococcus which when injected into calves and guinea-pigs brings about symptoms resembling those of scarlet fever. He has found a similar organism in vesicles on the teats of cows to which an epidemic of scarlatina has been traced. Edington and Jamieson have isolated a bacillus which is described as 1.2 to 1.4 micromillimetres long and .4 micromillimetre in width. The bacilli are found in the blood of scarlet fever patients during the first two days only, and in the desquamating epidermis after the twenty-first day. Inoculation upon rabbits caused fever, erythema, and a subsequent desquamation. Shakespeare in this country has confirmed these observations. His account of certain experiments is interesting: "A calf was inoculated and at the same time given some of the culture in milk. The calf was in good health at the time and had a temperature of 99.5° F. Six hours from the inoculation the calf developed great sickness, and the temperature, taken in the axilla, registered 103° F. The calf was left for the night, but in the morning was found dead. Small portions of the spleen and kidneys were placed in Koch's jelly and developed the characteristic bacilli. With this a second calf was inoculated when one day old. The inoculation was done with scrupulous care, and a previous examination showed no bacilli in the calf's blood. His temperature in the rectum was 99.6° F. The inoculation was done at 6.30 P. M. The following morning the temperature was 104° F. There were sickness, great prostration, diarrhœa, and soreness of the throat. In the afternoon the skin of the thorax, upper abdomen, and inner sides of the fore legs presented a general redness which increased toward evening. By the next day the animal was better and continued to improve. On the sixth day desquamation set in." The growth of the bacillus used in these experiments is, in cultures, very rapid, and this is of interest in view of the short incubation period in scarlatina.

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[1] *Practitioner*, July, 1894. [2] *British Medical Journal*, June 3, 1894.

[3] *Pester medicinisch-chirurgische Presse*, v. p. 990.

[4] *Internationaler klinische Rundschau*, Nos. 6 and 7, 1889.

Doehle[1] has observed in the blood of 5 scarlet fever patients two distinct parasites: (1) Small, flat, spherical corpuscles, measuring 1 micromillimetre, provided generally with a whiplike appendage of about the same length, which has a bulbous extremity; (2) corpuscles made up of two nuclei surrounded by a clear zone two or three times as large in area as the nuclei. This zone is finely granular and contains pigment granules. Movement in these cells occurs by contraction of the protoplasm. They may be outside or inside the red corpuscles. The author claims to have observed these parasites in the blood of measles and smallpox.

These illustrations afford an idea of the diversity of the bodies described as the germ of scarlet fever. Before we can accept any one of them as expressing the truth many control experiments must be brought forward in substantiation.

Scarlatina in the Lower Animals.—For a long time it has been a question whether there is a disease of lower animals corresponding to scarlet fever in man. The knowledge of the unity of smallpox and vaccinia has given additional interest to this question. Scarlatina is said to have been observed in dogs, cats, swine, horses, and cows. Heim[1] states that a dog which had lain in the same bed with a child who had scarlatina had a fever with a scarlatiniform rash which terminated in desquamation. The greatest interest of this question is as to whether scarlet fever exists in cows, for if it does we can readily see how the milk from infected animals may spread the disease to man.

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[1] *Revue mensuelle des Malades de l'Enfance*, July, 1894.

An epidemic of scarlet fever occurred in London in 1885 which has become historical as the "Hendon outbreak." The source of this epidemic was traced to a herd of cows which was affected with a contagious disease that could be inoculated upon healthy cows and man. From ulcers upon the udders Klein isolated an organism which he thinks identical with one he had obtained from human beings affected with scarlet fever. Others who have investigated the Hendon disease have failed to agree that the malady from which the cattle suffered was scarlatina. Hill[2] reports an outbreak of scarlatina at Sutton Coldfield, where all the homes invaded had the same milk supply. At the dairy from which the milk was obtained no case of human scarlet fever could be found. One cow which had recently calved and had been in the herd only a short time was in poor condition, and indications of recent ulcerations were found on her teats. The authorities declined to interfere. Soon a number of fresh cases of scarlatina appeared, and on a second visit to the dairy the cow was found to be desquamating in extensive patches. There was an ulcer on one teat and an eruption on the udder. A second cow presented indications of the same condition. The dairyman voluntarily ceased selling the milk and no further cases arose.

In August, 1892, an epidemic in Glasgow[3] was traced to the milk supplied from a certain farm. At this farm a child was found suffering from scarlet fever, but the date of sickening made it probable that the child was one of the victims, and not the source from which the milk was poisoned. The cows were found to be suffering from a teat eruption. Lymph and crusts were sent to Klein, who found a streptococcus resembling one which he had isolated from the Hendon outbreak. Lymph from these cows inoculated on calves produced two different eruptions, one of which was vaccinia, and the other of specific character, but entirely distinct from vaccinia. These instances serve to illustrate what seems to be the belief of the day, that there is a disease of cows the virus of which is capable of causing scarlet fever when introduced into the human being. It must be said that by no means all authorities are agreed on this subject. The practical point for the physician is that in all epidemics the origin of which is obscure the milk supply should be carefully scrutinized.

PATHOLOGICAL ANATOMY.—The most characteristic anatomical changes of scarlet fever are found in the skin and mucous membranes. Though a great number of pathological conditions are found in the course of scarlet fever, they have no essential relation with this malady, but are often present in other infectious diseases. An exception may be made in the case of nephritis, which occurs with such frequency as to deserve a position as one of the most important of the anatomical changes found with scarlatina. If seen in the commencement, the rash of scarlet fever is found to begin as small, pale red spots. In the course of a few hours these become confluent. The affected integument then presents a uniform scarlet background dotted thickly over with minute points of a darker hue. The skin has a swollen, œdematous appearance. On pressure the red color may be made to disappear, but when the rash is at its height there usually remains behind a faint yellowish staining of the surface. Sometimes it happens that there are points of a more purplish color which pressure will not dissipate, due to small hemorrhages into the skin, and in rare instances quite large areas are involved in the hemorrhages. The small red dots which are seen on the scarlatinous skin may become so much elevated as to constitute small papules, or in rare instances minute vesicles appear upon the skin.

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[1] *Cyclopedia of the Practice of Medicine*, Von Ziemssen, vol. ii. p. 166.

[2] *British Medical Journal*, July 18, 1892.

[3] *Ibid.*, January 7, 1893.

Microscopically the efflorescence is found to be due to a dilatation of the capillaries of the skin caused by paralysis of the vascular walls. In looking at a section one is struck by the fact that the epidermis and papillary body are folded, while the cutis is stretched and relatively shortened. Unna[1] explains this by stating that while the cutis was engorged the epidermis was gradually stretched, and that when by the section the cutis was allowed to recontract, it could not readily follow. The fact that the cutis is able to contract, he thinks, shows that there was not a true œdema of the skin. There are no indications of an inflammation in the strict sense of the word. When the eruption is at its height parakeratosis can be noted in the epidermis. Unna does not regard this as depending on the paralysis of the bloodvessels, but rather as a result of disturbance of the vasomotor centres, for the same parakeratosis is to be seen in *scarlatina sine exanthemate*. The darkened points mentioned above are due to an unusual dilatation of the subepithelial capillaries. These may represent small emboli due to the localization of the scarlatinal poison. Unna believes that it is from these points that the hemorrhages arise. Sometimes an interstitial œdema occurs in the neighborhood of the follicles, which in life causes the form of scarlatina known as *scarlatina papulata*. The exfoliations and other alterations in the epidermis are, according to Unna, the direct results of the action of the poison of scarlet fever, and are not to be regarded as arising from a true inflammation of the skin.

The alterations which arise in the throat are even more constant in scarlet fever than the skin eruption. Some[2] have gone so far as to assert that the essential point in diagnosis is the tonsillitis, as cases are extremely rare where it does not exist.

In its mildest form the angina presents itself as a uniform redness of the soft palate, with anterior palatine arches, and tonsils. If the process is of more severity, the red color is of a deeper hue; there are [illegible] of the affected parts and a muco-purulent discharge; [illegible] swollen and may rupture, leaving shallow ulcers. [illegible] over the tonsils at the angles of the jaws [illegible] pressure. In more severe cases the redness and injection of the mucous membrane extend into the mouth and nose.

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[1] [illegible] Dr. J. [illegible] Achte Lieferung.

[2] [illegible] Jan. 8, 1883.

The morbid process in the tonsils may result in an interstitial inflammation with great enlargement, and even the formation of abscesses. In ordinary cases there is little if any involvement of the larynx, but in severe cases the laryngeal mucous membrane may be affected to such a degree as to cause stenosis or abscesses.[1] When the inflammation falls with peculiar intensity upon the tonsils, there may result gangrene of a part or a whole of these organs. In cases of the greatest severity the inflammation extends from the fauces to the cellular planes of the neck. This is accompanied by great infiltration, swelling, and brawniness of the tissues. In most of these cases the cellulitis results in larger or smaller collections of pus. The infiltration may cause such interference with nutrition that large masses of tissue slough. On the separation of such gangrenous masses the muscles, vessels, and deeper structures of the neck may be exposed. If a large vessel be involved in the slough, rapidly fatal hemorrhage may occur.

A false membrane is not an infrequent accompaniment of scarlatinal angina. It is sometimes confined to the tonsils, but may involve the whole pharynx as well as the larynx and nose. It has long been a question whether such membranes represent simultaneous attacks of scarlatina and diphtheria. The discovery of a specific bacillus in association with diphtheria has done much toward the solution of this question. Recent investigations have shown that in a large number of the membranous throat affections accompanying scarlet fever the bacillus of Löffler cannot be found. Williams[2] in 35 cases in which a membrane was in the throats of scarlatinous patients found Löffler's bacillus in 12. In cases of pseudo-membrane which are not diphtheritic various micro-organisms have been found. Booker[3] has reported examinations of the membrane from the throats of scarlet fever patients. In none was Löffler's bacillus present. In all he found a streptococcus which differed from the streptococcus of erysipelas principally in that it did not live so long in culture media. Examinations made by Jackson[4] and others by Councilman[5] also showed streptococci. Bourges[6] found in 17 cases of pseudo-membrane with scarlet fever in some a streptococcus, in others the *staphylococcus pyogenes aureus*, the *bacterium coli commune*, and the *staphylococcus pyogenes albus*.

As Weigert has shown, the essentials for the existence of a false membrane are a sufficient necrosis of the epithelium and a fibrin-containing exudate. Reasoning from this fact and the observations mentioned above, we arrive at the conclusion that the false membrane which occurs with scarlet fever does not necessarily imply that diphtheria is present as a complication: such a condition forms no necessary part of the morbid process of scarlet fever, but is often due to the action of bacteria which have been secondarily engrafted on the already inflamed throat.

In a very large majority of all scarlatina cases nephritis of one or another occurs. This nephritis is of the type known as erulo-nephritis. In many cases the involvement of the kidney is of slight degree, while in some cases it progresses till a marked of parenchymatous nephritis results. Klebs was the first to draw ion to the frequency with which scarlatinal nephritis was a glom- r affection. He found the only noticeable condition to be the accu- tion of small angular nuclei and a finely granular matter in Bow- s capsules. More recent observers have found the glomerular tion, but it is not necessarily the only change. Klein finds the nges to consist in increase of the nuclei covering the glomeruli, line degeneration of the tunica intima, and multiplication of the i of the tunica media of the minute arteries, leucocytal infiltration g the course of the vessels. and parenchymatous changes the inten- of which depends on the degree he infiltration of the leucocytes. any observers describe also a marked increase in the interstitial tissue, l ascribe to it a part in the production of the other changes. In this nnection it is interesting to note that Fenwick[1] has extracted from ne spleens of rapidly fatal cases of scarlet fever a substance which introduced into the circulation of animals tends to produce an acute parenchymatous nephritis.

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[1] *La Semaine médicale*, May 7, 1893.

[2] *American Journal of the Medical Sciences*, Nov., 1893.

[3] *Johns Hopkins Hospital Bulletin*, Oct. and Nov., 1892.

[4] *Boston Medical and Surgical Journal*, Aug. 17, 1894.

[5] *Ibid.*

[6] "Les Origines de la Scarlatine," *Thèse inaugurale*, Paris, 1891.

SYMPTOMS.—It is a very difficult matter to give a comprehensive yet succinct account of the symptoms of a disease which presents so variable a course as scarlatina. It will perhaps be best for purposes of description to divide the affection into those cases which have an ordinary or typical course, those which are malignant, and those in which variations from the normal course of the malady are to be noted.

The Ordinary Form.—As a rule, in the period of incubation there are no symptoms or they are so slight as to pass unnoticed. Sometimes, however, slight malaise is complained of if the patient be old enough to give expression to his sensations, and if the temperature be taken a slight evening rise may be detected. The stage of invasion is ushered in abruptly, so that commonly the exact time of the beginning of illness can be stated. In a large proportion of cases chilly sensations are experienced in the commencement of an attack, and in some a decided rigor. In young children it may happen that a convulsion is the first symptom of illness. The temperature rises rapidly, and in a few hours attains a considerable degree. It may reach 102°, 103°, 104° F., or even higher. The increased temperature is accompanied by those symptoms which usually mark fever from any cause, such as headache, loss of appetite, flushing of the face, sparkling eyes, and thirst. Coincident with the elevation of the temperature there is an increase in the rapidity of the pulse, and it is a thing to be noted that the pulse rate in scarlet fever is out of proportion to the height of the fever.

Vomiting is one of the most important of the early symptoms of scarlet fever. It may occur but once, but it is apt to be repeated during the first day. Smith has found vomiting present in 162 out of 214 cases of scarlet fever. Thomas states that it occurs more frequently as an initial symptom of scarlet fever than with any other disease of childhood except smallpox and pneumonia. Vomiting in the early period of scarlet fever has been variously interpreted. It is generally regarded as a nervous phenomenon, but by some it is thought to indicate a catarrhal condition of the stomach. In rare instances vomiting may continue through the course of the disease, constituting one of the most embarrassing symptoms, as it may seriously interfere with the administration of food and medicine. In a certain proportion of cases there is a mild diarrhœa, which usually ceases after a day or two. In a small number of the more severe cases this symptom assumes alarming proportions. At this period of the disease the tongue is usually coated with a thick whitish fur, through which the swollen hyperæmic papillæ may be seen protruding. From the very onset of the malady there is sore throat. In adults and older children this is evinced by difficulty and pain on deglutition. The different characters presented by the throat have been sufficiently dealt with under the heading of Pathological Anatomy (page 588). In the ordinary cases it is only the less severe forms of throat trouble which are found. The lymphatic ganglia over the tonsils at the angle of the jaws are enlarged and tender on pressure. There is little evidence at this period of any catarrhal involvement of other mucous membranes.

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[1] *British Medical Journal*, Aug. 19, 1894.

The symptoms presented in the stage of invasion on the part of the nervous system vary considerably in different cases. As already mentioned, it is not uncommon to have one or more convulsions, and it is worthy of note that, occurring at this time, they are not of such grave significance as when seen at a later date. Nearly always from the first there is marked prostration. Often the patient lies in a dull, apathetic state. In other cases restlessness with twitching of the limbs occurs.

The Rash.—Generally before the end of twenty-four hours from the initial symptoms the rash makes its appearance. Sometimes it is not developed till the second day, and in very rare cases not till a later period. The rash appears first on the neck, chest, shoulders, or lateral parts of the face in rather ill defined patches. The patches rapidly coalesce, till in the course of a few hours, nearly always less than half a day, the whole body is covered. The lips and alæ nasi generally escape the rash, and when the cheeks are brightly tinged the contrast between the scarlet and white portions of the face gives a peculiar and striking appearance. The characters of the rash have already been mentioned. It begins as small points of a red color, but in a very short time becomes a diffuse scarlet erythema, with innumerable points of a deeper hue scattered over the surface. The rash as usually seen very closely resembles the appearance caused by the application of a mustard plaster. In some cases where the rash is rather mild the original red points may remain discrete. This is said to be most prone to happen on the abdomen. The rash generally is best developed on dependent parts and regions kept warm, as on the back and at the flexures of the joints. Although the involved surface may appear smooth to the eye, yet if the hand be passed gently over it a fine roughness can be detected. The scarlet color can be made to disappear by pressure, but returns as soon as the finger is raised. If sufficient irritation of the capillary walls be produced, as by stroking the skin roughly with a pencil, a white line persists for some moments. At one time this phenomenon was supposed teristic of scarlet fever, but we now know that it is common y erythemas. The surface involved is hyperæsthetic, and a sen- of itching and burning is often experienced.

time required for the full development of the rash varies. In ases it may reach its height on the first day. In other cases the oom of the efflorescence is not attained till the second, third, or ourth day, and in rare cases at a later date. When the eruption its height the skin is tense and swollen and has an œdematous look, cially about the eyelids.

While the rash is reaching its full development the other symptoms increasing in severity. The temperature in ordinary cases may h its maximum as the rash comes out, a height of 105° F. being not ommon. It may remain at this point till the rash has attained its and then gradually decline. At other times there is a steady ease in fever *pari passu* with the progress of the eruption toward bloom. In rather mild cases, when the rash is not fully developed the second day, it often happens that in the morning of that day re is a decided remission in the febrile movement.

The tongue by the fourth day has usually lost its coating and has come of a bright red, often glazed, color. It is studded over with wollen papillæ (strawberry tongue).

The throat symptoms increase in severity. Besides the redness and œdema already noted, the tonsils become covered with a layer of yellow-h pus. The inflammation not infrequently extends forward into the ccal cavity and upward into the nose, from which there is a mucopurulent discharge.

Usually by the time the disease has reached its height the vomiting and diarrhœa which may have been present at first have ceased, and constipation exists. The nervous symptoms also increase, and there may be delirium with restlessness or sometimes profound somnolence. The pulse remains rapid.

The urine at the height of the malady is high colored, loaded with urates, and diminished in quantity. In the majority of cases at this time at least a trace of albumin can be found, and often it is considerable in amount. Some authors (as Bartels and Thomas) ascribe the albuminuria of this period to the pyrexia, while others (Steiner and Eisenschitz) think that it indicates an organic lesion of the kidney. It is the latter view which is now accepted. Indeed, this is the only logical opinion, for it often happens that there are in the urine evidences of renal mischief other than albumin. Red and white blood cells and hyaline and blood casts can frequently be detected. In many similar diseases it has been shown that nephritis can exist early in the illness, and Klein has found glomerulitis in scarlet fever as early as the second day. Obermüller first called attention to the presence in the urine of scarlatinous patients of peptone. Arslan,[1] after extended observations, thinks this is a symptom of the greatest importance. His conclusions are as follows: (1) No peptone is found in mild cases; (2) the urine contains peptone in grave cases associated with complications, the occurrence of the latter being preceded by peptonuria; (3) the presence of considerable quantities of peptone is an unfavorable sign; (4) the presence of peptone is not influenced by albumin or by the condition of the pulse or temperature.

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[1] *Gazette médicale de Paris*, Feb. 25, 1894.

The eruption stays out in full bloom from a few hours to one day. It fades from the body in the order of its appearance, often lingering longest on the backs of the hands and feet. Generally by the end of the third day from the beginning of decline the rash will have entirely vanished. The whole duration of the eruption is from three to seven days. Octerloney,[1] by counting from the commencement of fever to its subsidence, found the average duration in 40 cases to be six and a half days.

With the fading of the rash all the other symptoms grow better. The fever falls by lysis, the throat heals, the appetite returns, the nervous symptoms disappear, and the urine grows more abundant and of lighter color, while any albumin which it may have contained usually disappears.

Desquamation may begin as early as the third day, though most often not till about the time of the fading of the rash. In rare cases it has first appeared at a considerable period after the termination of the eruption. The character and amount of the desquamation depend in large degree upon the severity of the preceding eruption. Where the rash has been slight the desquamation may be furfuraceous. In typical cases, however, it occurs in large lamellæ, and in severe cases, in regions where the epidermis is thick, as on the hands, perfect casts of the member may be exfoliated. Desquamation usually continues for a week or ten days, though it may be prolonged, and in some cases a second or even third desquamation has occurred.[2]

By the time desquamation is completed convalescence is well established and all morbid symptoms have passed away, save that the pulse is apt to continue rapid, sometimes until convalescence is far advanced.

Even with the beginning of convalescence the disease cannot be treated as though it were a thing of the past, for, as we shall see, although an attack may have been mild, the patient is more or less liable to serious sequelæ. Such unfortunate accidents are especially liable to result if recovery has been too readily assumed and the safeguards which should have been thrown around the convalescent have been too soon relaxed.

Between the ordinary form of scarlet fever which has been outlined and the grave form to be described there are all grades of severity. An effort has been made in the description to indicate this and to keep constantly before the mind of the reader the marked variations in the course of the malady.

Malignant Forms of Scarlatina.—In almost every epidemic of scarlet fever there occur a certain number of cases which may properly be called malignant on account of their great tendency to a fatal issue. In some epidemics the number of these cases is especially striking, so that we are led to believe that at such times the poison of scarlet fever is of unusual virulence.

In one form of malignant scarlatina the intoxication is so severe that death may result on the first day of the period of invasion, the patient overwhelmed before the eruption has manifested itself. Where atal termination is not so immediate, the symptoms from the first ate the gravity of the case. The manifestations on the part of the ous system are severe. There are intense headache, extreme restless- , delirium, convulsions, and not uncommonly the patient rapidly falls a state of coma. The fever reaches an untoward height, a tempera- e of 107° F. and even higher having been observed. The pulse attains h a degree of rapidity that it may be impossible to count it. Great ritability of the stomach is a frequent symptom, and the dangerous dition may be rendered even more unfavorable by constant vomiting. those who survive the rash is slow in coming out, and is frequently a more dusky hue than is observed in the ordinary cases. In the all proportion of cases which recover the whole course of the illness apt to be lingering and tedious.

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[1] *System of Medicine*, Pepper, vol. ii. p. 506.

[2] *Cyclopædia of the Diseases of Children*, Keating, p. 567.

Another form of scarlatina of marked malignancy is the hemorrhagic type of the disease. The symptoms are severe from the onset; hemorrhages from the various outlets of the body occur. There may be epistaxis, bleeding from the gums, and hæmaturia. When the eruption appears it assumes a hemorrhagic form. At first petechiæ are seen in the skin, but these rapidly grow larger, and the entire surface may be involved in large hemorrhagic areas. Death often takes place on the second or third day. Post-mortem parenchymatous hemorrhages are found to have occurred in the various organs.

Scarlatina anginosa should be classed among the malignant varieties of the disease. The stress of the attack seems to fall upon the throat. The mucous membrane of the throat presents from the beginning much swelling, and is apt to show a cyanotic or livid hue. A membranous exudation forms, which may extend into the larynx, mouth, or nose. The lymphatics of the neck rapidly enlarge. Necrosis or gangrene of the affected structure results, and the breath has an extremely fetid odor. The patient lies semicomatose, the picture of one suffering from profound septicæmia. If death does not terminate the scene too early, there may be an extension of the inflammation to the cellular planes of the neck. The tissues may become swollen to such a degree that the neck is even with the chin. There is much infiltration and brawniness, so that the mouth can no longer be opened to inspect the throat. Difficulty in breathing may result from the swollen condition of the tonsils and the pressure of the infiltrated tissues of the neck, or from an extension of the trouble into the larynx. The cellulitis may lead to the formation of abscesses of the neck or gangrene of large portions of tissue may result, the separation of which may lead to fatal hemorrhage.

Variations from the Ordinary Course of Scarlatina.—It has been indicated above that scarlet fever presents a great number of variations from what we may term the normal course of the disease. Although it would be an endless task to catalogue all, it is necessary to consider some of the more important of these abnormal forms.

Though no case of scarlet fever can be regarded as entirely free from danger, there are many cases which are extremely mild. In these cases the febrile symptoms are slight, the temperature not rising much above 100° F.; the nervous symptoms are absent; the involvement of the throat is limited to a slight catarrh, with some injection and redness of the tonsils and fauces. The rash is never very distinct, and is not of that bright scarlet color which is so characteristic of the eruption in its typical form, but has more of a pink hue and fades in a day or two after its appearance. The patient does not feel ill enough to go to bed. Under proper treatment these cases run a course as favorable as the symptoms are mild, but, unfortunately, it is this class of cases which is often diagnosed "scarlet rash," and to which the name scarlatina is applied by ignorant persons under the impression that this term implies an eruption entirely distinct from scarlet fever and not dangerous. These mild cases sometimes are followed by the sequelæ of scarlet fever, and demand as much care as the more severe types of the disease.

Cases of scarlatina have been reported in which throughout the illness there was no rise in the temperature. It is very likely that many such instances have been cases of scarlatinoid erythemas. It is not impossible, however, that scarlatina may run its course without fever, since the same apyretic course has been seen in typhoid fever. Fiessinger[1] in a paper on this subject draws these conclusions: (1) There is a form of scarlet fever in which the fever is entirely absent. (2) This form may be observed in the same epidemic and alongside the grave and pyretic forms; it is contagious, and may give rise to the ordinary form of the disease, complicated with Bright's disease or with pseudomembranous angina. (3) There is no local symptom to differentiate the apyretic from the pyretic form. (4) The pulse is not always accelerated in the apyretic form. (5) The apyretic form is characterized by the absence of general phenomena.

The diagnosis of this form of scarlatina from other erythemas must be very difficult, and could be made only in the presence of an epidemic or when some of the well known sequelæ of scarlet fever follow.

Most authors are agreed that scarlet fever without the rash may occur. During the epidemic cases of sore throat of greater or less severity are observed, after which desquamation or nephritis follows. The writer knows of a young medical man who had never had scarlet fever, and who, while attending some severe cases of scarlatina, was seized by a chill followed by an intensely sore throat. On the second day the urine became bloody and a hemorrhagic nephritis was found to be present. In this case no desquamation was observed. In speaking of this subject under the heading Immunity, page 583, attention was called to the fact that the true scarlatinal nature of such attacks, however probable it may seem, is generally open to question.

Cases in which the rash is present without the sore throat have been reported, but their occurrence is doubted by many authorities, and it seems to the author justly so, for we know that there are a number of erythemas which very closely simulate scarlatina, the chief differential point being the absence of sore throat.

In some cases of scarlatina the fever is peculiarly prolonged, and the patient falls into a low condition to which the term typhoid is applied. In such cases the local lesions are not sufficiently severe to account for the long continuance of the fever. The temperature is high, and may continue in a more or less remittent form for several weeks. The nervous symptoms are marked and peculiar. A low form of mental hebetude develops, and the patient lies partially unconscious with a dull, apathetic expression, his hands aimlessly fumbling with the bedcovering. The tongue and lips are dry and cracked and sordes accumulates on the teeth. The likeness to typhoid fever is still further carried out by the fact that there is marked enlargement of the spleen and there may be diarrhœa. It is stated that after death in some of these cases Peyer's patches and the mesenteric glands have been found enlarged.[1]

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[1] *Gazette médicale de Paris*, March 4, 1894.

Thomas and Gumprecht[2] have recorded cases in which the fever persisted for from eight to fifteen days beyond the usual period, but without serious symptoms. In these cases defervescence occurred more or less abruptly, and at no time was there hyperpyrexia. The cause of this long continued fever seemed to be streptococcus infection which had occurred through the tonsils.

Bouveret[3] has noted in some cases a secondary hyperpyrexia which occurred on the ninth or tenth day and after the rash had disappeared. The temperature rose rapidly to 105° or 106° and was accompanied by grave nervous symptoms.

Talamon[4] refers to cases in which there was hyperpyrexia even from the first day, which persisted for a period of eighteen or twenty days. The fever was not dependent upon any local lesion, but was the essential element and constituted the entire danger. Talamon found that cold affusions as ordinarily practised are worthless, in such cases the only efficient treatment being full cold baths at frequent intervals. In this connection the writer would mention certain cases that he has seen which were marked from the first by a hyperpyrexia which could not be controlled even by cold baths, the patients rapidly dying from the effects of the high degree of fever.

Relapses.—Reference has been made to relapses of scarlatina under the heading Immunity, page 583. Here it is only necessary to mention that the form to which Thomas has given the name pseudo-relapse varies in its course considerably from the ordinary form of the disease. The rash may appear only on limited regions of the body; when it affects the face the region about the mouth and nose is not exempt. The eruption does not reach its full development on all the affected portions at nearly the same time, but progresses in an irregular manner. The behavior of the temperature during the pseudo-relapse is irregular, and the maximum of the rash and the highest fever do not coincide.

Variations in Type.—In general it may be said that marked variations in the course of scarlet fever are caused by the complications which may arise. This part of the subject will be more particularly referred to in speaking of Complications, page 597.

The most important variations which occur in the local symptoms of scarlet fever are the different forms which may be presented by the eruption. It may happen that the rash develops first upon some unusual site, as the abdomen, back, or limbs. Again, it may appear on the whole surface at the same time. The rash may occupy only certain regions, as one half of the body or the upper portion, while the rest is free. It has been noted occurring on very limited areas, as upon a small part of the belly, on the neck, or in the flexures of the joints. Some authors state that scarlatina is prone to avoid paralyzed limbs. The minute characters of the eruption may also vary. It may not be of the usual scarlet color, but a lighter red, and in cases where for any reason there is marked sluggishness of the circulation a very dusky hue may be noticed. The rash instead of becoming confluent may occur as small red macules. Reference has already been made to the fact that in most cases on passing the hand over the surface a roughness can be felt. In some cases there are more decided elevations of the skin, which can be detected by the eye as numerous minute, acuminate papules; to this form the term papular scarlatina has been applied. There may occur over the surface, especially in regions kept warm, a crop of miliary vesicles constituting vesicular scarlatina. Should the contents of the vesicles become purulent, we have the form of the disease which is called pustular scarlatina.

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[1] *Cyclopedia of the Practice of Medicine*, Von Ziemssen, vol. ii. p. 269.

[2] *Deutsche medicinische Wochenschrift*, July, 1888.

[3] *Revue de Médecine*, April, 1893.

[4] *La Médecine moderne*, Sept. 15, 1893.

Those grave forms of scarlatina in which extensive hemorrhages occur in the skin have been already described. In other cases small petechiæ may be observed at various points upon the surface, and this feature in itself does not indicate malignancy of the attack.

Such is a description of the most commonly observed departures from the usual course of scarlatina. We must now consider the complications which may attend and the sequelæ which may follow attacks of the malady.

COMPLICATIONS AND SEQUELÆ.—It may be said that in scarlatina the complications are commonly the results of unusually intense morbid action on the part of organs which are affected in the normal course of the disease. The line between complications and sequelæ is not sharply drawn, and that which began as a complication may by long duration become a sequel. There is no stage of scarlet fever which is free from liability to complications. While they are most frequent in severe epidemic and grave cases, still, even in the mildest case serious complications may arise. It may here be mentioned that just before a complication of some important organ is discovered the rash, which has been out in full bloom, will suddenly fade. This phenomenon is popularly known as "striking in," and among the laity, and formerly even in the profession, the complication which existed was regarded as the direct attack of the rash upon the affected organ. Hebra first showed that "striking in" was to be regarded as the result and not the cause of the complication.

Among the most important as well as the most frequent complications of scarlatina the affections of the nervous system deserve a place. Those malignant cases in which the patient falls almost at once into coma have been considered, as well as the delirium which may arise from hyperthermia. Convulsions occur chiefly at the beginning and toward the close of an attack of scarlet fever. In the first instance they are usually due to the action of the scarlatinal poison upon the nervous centres, while in the second they are often an accompaniment of the condition known as uræmia. Convulsions may also indicate the onset of a grave complication, and may thus occur at any period of the disease. All the symptoms of an acute meningitis may be present, and it is often a matter of much difficulty to decide whether that rare complication really exist in cases presenting such a train of symptoms a post-mortem examination has not infrequently shown an absence of the anatomical features meningitis. A case[1] has recently been reported in which persistent ugh set in on the third day. The paroxysms came on every two ree minutes, and were so severe that eating, drinking, and sleeping e interfered with. The attack lasted seven days, and terminated in very.

The severe forms of angina which occur with scarlet fever have been scribed. In addition to what has been said, it may here be mentioned t necrosis of the tissues may result in perforation of the soft palate[2] an external opening into the pharynx, so that food cannot be swalwed.[3] In cases of severe cellulitis of the neck the inflammation may tend down into the mediastinum. A very frequent complication of carlatina is membranous deposit in the throat. The discussion of the gnificance of this symptom will be found under the heading Diagnosis page 604).

The fact that the Eustachian tubes open into the pharynx makes inflammation of the middle ear a common complication. The inflammation from the fauces creeps up into the tympanic cavity, and, as the Eustachian tube is very often occluded, the products of inflammation have no means of escape. By the accumulation in the middle ear are caused pain, increase in fever, and bulging of the membrana tympani. When the Eustachian tube is completely occluded the pent-up secretions can escape only by a perforation of the drumhead. After this has occurred in favorable cases a purulent discharge exists for a shorter or longer time, and then the opening in the membrane heals with very little permanent injury to the ear. Unfortunately, in a great many cases this happy result is not obtained. If pus be for long pent up in the tympanum, permanent injury may be wrought to the delicate structures there contained, necrosis of the small bones may result, or the inflammation may extend to the mastoid cells. The mucous membrane which lines the bony walls of the tympanum largely contributes to their nourishment, and when this function is disturbed by the inflammation necrosis of the bone may result. This is a serious condition, as the anatomical situation of the tympanum renders it easily possible for other important structures to be involved with it. Septic thrombosis may occur in the adjacent sinuses or veins; meningitis or abscess of the brain may result. Even if no such serious accident follows, total destruction of the drumhead with loss of the ossicles and a chronic purulent discharge may be the final outcome. Where a gangrenous condition of the fauces has existed, gangrene has been observed to extend up the Eustachian tube and so involve the ear. When the ear is affected during an attack of scarlet fever in children who are old enough to speak, pain will be complained of; in younger children it will be evinced by putting the hand to the ear or by pressing the ear against the pillow. Such actions on the part of children should always ensure an examination of the ears.

It has been mentioned that in cases of any severity there is often more or less involvement of the Schneiderian membrane. Under ordinary circumstances the morbid process gives rise to a purulent discharge, and resolves without any permanent damage to the mucous membrane. At times, however, ulceration occurs and alarming hemorrhage may result.

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[1] *Lyon médical*, Sept. 11, 1893.

[2] *The Medical Week*, Nov. 9, 1894.

[3] *System of Medicine*, Pepper, vol. i., p. 512.

Inflammation of the larynx is most common where scarlet fever is complicated by diphtheria. Stenosis of the larynx may ensue from the amount of pseudo-membrane formed or from coincident œdema. Sometimes ulceration of the larynx results.

Bronchitis is one of the rarer complications of scarlet fever.

Both croupous and catarrhal pneumonitis may occur during the course of scarlatina, and are more likely to prove fatal when appearing during a nephritis than when manifested earlier in the disease. Gangrene of the lung has been observed. Œdema of the lung is a serious accident that may arise at any period of the disease. It is usually accompanied by sudden failure of the heart's action. A more important complication is pleuritis, which may develop as secondary to some lung trouble, but more often occurs independently, coming on during desquamation. Pleurisy may attain considerable proportions without causing symptoms which would attract attention to its existence, but its presence is usually manifested by cough, difficult breathing, and pain on the affected side. The pleuritis of scarlet fever, just as the other serous membrane inflammations which complicate the disease, shows a tendency to become purulent. Such empyemas run the same tedious course seen in those which arise under other circumstances.

The involvement of the buccal mucous membrane which is observed in scarlatina amounts usually only to a catarrh, but there may occur quite severe ulcerations of the cheeks and gums, and in rare cases the gangrenous condition called noma.

The symptoms on the part of the gastro-intestinal mucous membrane may be severe. Attention has already been called to the fact that in some cases vomiting is persistent and becomes a serious complication. Diarrhœa may also be a grave symptom. In rare cases the gastro-intestinal disturbance may be so intense early in the disease as to cause death. In such cases it is possible that a large dose of scarlatinal poison has been taken in with the food or drink, and has come in the first instance into contact with the gastric or intestinal mucous membrane. In the latter part of an attack of scarlet fever dysenteric symptoms may arise—tenesmus, pain on pressure over the colon, and bloody stools.

The circulatory apparatus is liable to attack. The heart action is usually very rapid and it may become weak and irregular. Post-mortem examination shows that the cause for this is often found in a fatty degeneration of the muscular fibres of the organ. In life such a condition, by the weakness of the walls of the heart which it occasions, may lead to acute dilatation. Fibrinous coagula sometimes form within the cavities of the heart, and pieces of these, washing away in the blood stream, may give rise to embolism of the peripheral arteries. It not infrequently happens that during scarlet fever murmurs are heard over the cardiac region. These murmurs present different characters and depend on various causes. Some are hæmic murmurs. Some of them are no doubt caused by a relative insufficiency of the valves due to the weakened and dilated condition of the walls of the heart. Such abnor-

und ppear as convalescence advances. In other cases the ur persists and other signs of organic valvular lesion develop. ombosis of veins has been reported as occurring as a complica- o scarlatina. When this takes place in the veins of the cerebrum ied train of nervous symptoms follows, the character of which will d on the vein affected. Inflammation of arteries may arise during course of scarlatina. Siredey[1] has reported such an occurrence in aorta. Inflammation of the pericardium, though not a common plication, is one which has been frequently observed. It manifests same symptoms and signs as when found under other circumstances. infrequently the accumulation in the pericardial sac is purulent.

Peritonitis, with accumulation of pus and adhesions between the stinal coils, is sometimes found with scarlet fever. The writer well embers a case in which all the symptoms of peritonitis—distention the belly with gas, constipation, vomiting, and marked sensitiveness pressure—came on toward the close of an attack of scarlatina. The rine was scanty with a trace of albumin and an occasional cast. So certain were those who had the case in charge that a septic peritonitis was present that it was proposed to open the belly for drainage. It was decided that the condition of the child was too bad to justify such a procedure. At post-mortem examination no trace of peritonitis was present, but there was a nephritis of such intensity that it seemed strange that the capsules of the kidney had not been ruptured by the enormous swelling of the organs.

The affection known as scarlatinal rheumatism is a synovitis coming on usually during the latter part of the period of eruption or the first of desquamation. It attacks most often the phalangeal, ankle, and wrist joints, but may involve any articulation. As a general thing, there is little swelling, but the joint is painful and tender. Some believe that this affection is really rheumatism complicating scarlet fever, but the writer does not believe that this assumption is necessary to explain the symptoms presented, and prefers to regard scarlatinal rheumatism as a synovitis due to the action of the poison of scarlet fever. It is thought by some authors that the presence of scarlatinal rheumatism increases the liability to valvular disease of the heart. Generally the inflammation of the joints subsides in a few days, but in rare instances a suppurative synovitis develops, with destruction of the joint. When large articulations are thus affected a fatal pyæmia is the frequent result.

Periostitis may complicate scarlet fever, and when severe may lead to necrosis of bone. Separation of the epiphyses of bones[2] is one of the rarer accidents which may occur during scarlet fever.

Myositis is an unusual complication. It may be manifested as a certain amount of infiltration into the muscle, with pain and difficulty of motion, or the process may go on to the formation of abscesses.

During the height of the eruption there sometimes occurs a conjunctivitis, though this is not a common complication. A keratitis may develop which may lead to the formation of an abscess or an ulcer of the cornea. Occasionally the whole cornea sloughs and the eye is destroyed by a panophthalmitis. A purulent panophthalmitis can also occur from a septic embolus lodging in the eye. When there is a diphtheritic complication in the throat the membranous inflammation sometimes attacks the eye and may lead to its destruction.[1]

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[1] *The Medical Week,* November 9, 1894.

[2] *Canadian Practitioner,* January, 1894.

That other infectious diseases may complicate scarlatina has been mentioned on a previous page. All the exanthemata have been observed in conjunction with it. Of course the gravity of the affection is added to by such complications.

Certain skin lesions may arise during the course of scarlatina. The most important are erysipelas, urticaria, herpes simplex, furunculus, and gangrene of more or less extensive areas.

Scarlatinal Nephritis.—Perhaps the most important complication of scarlatina is nephritis. By many nephritis is classed as a sequel, but if, as is generally believed, the nephritis really finds its origin in the slight affection of the kidney which occurs at the height of the eruptive stage, it is certainly more appropriate to consider it as a complication. As has been mentioned, if a careful urinary examination is made when scarlatina is at its height, it can usually be shown that there is present a more or less severe inflammation of the kidney. In the majority of cases this subsides with the decline of the malady, and if the case be properly cared for recovers without having caused any noteworthy objective symptoms. In a certain proportion of cases, on the other hand, the inflammation of the kidney progresses, and in the course of time gives evidence of its presence by severe symptoms. Although nephritis is more prone to occur in some epidemics than in others, there is no case of scarlatina so mild that it may not develop. Indeed, the very mildness of a case of scarlet fever may render the occurrence of nephritis more likely, because in such cases the necessary precautions are apt to be neglected. The writer has seen cases in which a diagnosis of "scarlet rash" had been made by an ignorant person, and the children allowed to be out of doors during the whole course of the disease, as they did not seem ill, in which a severe nephritis with general anasarca developed. The first noticeable symptoms of nephritis commonly manifest themselves in the declining period of scarlatina, during desquamation or immediately after it, though cases are reported in which nephritis is supposed to have first developed a number of weeks after an attack of scarlet fever. Catching cold has always been regarded as the chief determining factor in scarlatinal nephritis. It not infrequently happens that as soon as the severe symptoms attending the rash are past the patient is allowed to be up, and is thus exposed to injurious influences, among which exposure of the surface to varying degrees of temperature is certainly one. Probably a more important factor is posture and the increased work which the exertion of being up and around throws on the kidneys. In 179 cases which Gresswell[2] examined albuminuria returned in 130 after getting up, at times varying from twenty-four to thirty-one days after the beginning of illness.

In some cases the onset of symptoms attributable to nephritis is abrupt. The fever, which has declined to near the normal, will rise again, there will be headache, perhaps vomiting, restlessness, and a very small amount of highly albuminous and even bloody urine. In the ity of cases, however, the inauguration of the nephritis is more al. Perhaps the fever does not decline so rapidly as it should, or, ing reached a point almost normal, it may continue there, this small ee of fever being for the time the only indication that things are progressing favorably, or it may be the fact that the urine is growgradually scantier that first attracts the attention to the presence ephritis. Unless a careful examination of the urine has been made equent intervals, it may happen that œdema will be the first evince of renal mischief. Dropsy is very commonly first perceived in e eyelids or in the hands and feet; in those who have been constantly bed it may appear first upon the back. In a severe case the œdema tends all over the body, the skin is much swollen and pits on presre, and often where the swelling is greatest there will be tenderness. he œdema may affect other organs. Pulmonary œdema or œdema of he glottis may reach such proportions as to render breathing impossible. Accumulations of fluids in the serous cavities of the body may be so large as seriously to interfere with the function of important organs, as the heart or lungs. It occasionally happens that one of these internal dropsies is first to develop, and the anasarca appears only at a later date, or it has been noted that œdema of an internal organ—the lungs, for instance—has been the only manifestation of dropsy. Œdema after having persisted for a time subsides as the nephritis grows better, but where the the kidney lesion passes into a chronic form the œdema may also become chronic.

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[1] *Atlanta Medical and Surgical Journal*, March, 1891.

[2] *A Contribution to the Natural History of Scarlatina*, Gresswell.

The excrementitious products which should be eliminated in the urine accumulate in the blood during the nephritis, and often in such quantities as to give rise to alarming symptoms. The term uræmia is applied to this condition, and although it is a misnomer it is retained, because by long use it has acquired a definite significance. The symptoms of uræmia vary much in intensity. They may be manifested only as more or less severe headache, vomiting, restlessness, twitching of the muscles, or sudden dilatations and contractions of the pupils. In more severe cases convulsions occur, and these may be succeeded by coma. There is usually a definite relation between the uræmic symptoms and the quantity of the urine, the former becoming more severe as the latter grows less. It is worthy of note that children often bear uræmia better than adults, recoveries having been observed under the most unpromising circumstances.

The condition of the urine in scarlatinal nephritis varies greatly in different cases. In the milder cases it is slightly diminished in quantity, while in severe cases it may be as little as 50 c.c. in twenty-four hours, or anuria may exist for quite long periods. The specific gravity is higher than normal. The color is of a reddish yellow, or may be red or a smoky greenish hue from the blood which the urine contains. The amount of albumin varies from a mere trace to such a quantity that the urine solidifies on boiling. On standing there falls from the urine a more or less copious sediment made up of urates and uric acid and formed elements from the kidney in varying amounts. Renal epithelium may be found in differing states of preservation, some of the cells much swollen, others showing fatty degeneration. In most cases red blood corpuscles and leucocytes can be seen. The most significant signs of renal inflammation are the casts, of which several different forms may be found. Hyaline casts are nearly always present, and at times they are very long, flat, and convoluted, with the ends uneven, the so-called cylindroids. Epithelial casts also can generally be demonstrated, and when blood is present in the urine blood casts are formed. Although the results of a urinary examination usually afford the most certain evidence of nephritis, it sometimes happens that marked renal changes exist without the appearance of albumin or casts, or these may occur at one time and be absent at another examination. The writer recalls a case in which post-mortem there was found a very severe nephritis apparently involving the whole of both kidneys, in which in life the only changes in the urine were a slight diminution in quantity, a small amount of albumin, and an occasional hyaline cast.

The course of scarlatinal nephritis presents many variations. In ordinary cases in the course of a week or ten days the œdema and other symptoms have disappeared and convalescence is begun. Careful urinary examinations will often show traces of albumin and casts for long periods even in these favorable cases. In rare cases a small amount of œdema persists, the patient does not recover health, but becomes anæmic; the urine constantly contains albumin and casts; the heart becomes somewhat hypertrophied; and a chronic form of Bright's disease is established. When death occurs during an acute scarlatinal nephritis it is generally due to œdema of some important organ or to uræmic poisoning. Death may also occur from some acute intercurrent inflammatory trouble, as a pneumonia or pericarditis.

As has been mentioned, no sharp dividing line between the complications and the sequelæ of scarlet fever can be drawn. It is customary to apply the term sequelæ to those morbid manifestations which appear after the activity of the scarlatinal poison has presumably exhausted itself, as well as to those complications which persist after other evidences of the malady have passed away. Only the most common and important of the sequelæ can be here considered.

The inflammation of the throat may leave in its wake a chronic hypertrophy of the tonsils. A perforation of the soft palate or of the septum of the nose may result from local gangrene.

It has been mentioned that, owing to the inflammatory changes occurring in the ear as complications, a long continued purulent discharge may be a sequel. When necrosis of the bony structures of the tympanum has occurred, it may happen that serious intracranial mischief, such as abscess of the brain, develops even long after the original damage was sustained.

In the eyes total blindness may result from the severity of the affections caused by the scarlatinal poison. Chronic interstitial keratitis, iritis, and neuro-retinitis are among the important sequelæ in these organs.

Tubercular infection of the lung, larynx, bones, and lymphatic ganglia may follow in the wake of scarlatina, just as we see it developing after other acute affections.

Paralysis of various muscles or groups of muscles not infrequently remains after an attack of scarlet fever. This paralysis is of similar nature to that which comes on after diphtheria and other infectious dis-

Chorea in a number of instances has first manifested itself after . fever. When scarlatinal rheumatism has taken the form of a rative synovitis, permanent ankylosis of one or more joints may

ronic valvular heart troubles are not infrequent sequelæ of the ttacks of endocarditis which complicate scarlet fever. Owing to akening of the heart walls, it may happen that when the patient has recently experienced scarlatina has been up and around for le an acute dilatation of the heart develops with a relative insuf- y of the mitral valve. The writer thinks it probable that some reported cases of œdema coming on in the period of convalescence ut any kidney trouble are of this nature. Basedow's disease has observed to occur suddenly after scarlet fever.[1]

n the skin and its appendages sequelæ may follow. Erythemas ore or less diffuse have often been noted after desquamation has commenced. Kaposi believes that relapses are generally to be thus explained, rash representing a secondary erythema and not a scarlatinal recrudescence. Erythema nodosum, urticaria, herpes zoster, and localized angrenous conditions of the skin sometimes develop after scarlet fever. n alopecia more or less complete may follow, just as we find it after other infectious maladies, and in a few cases permanent canities has been reported.

After an attack of scarlatina there is often left a profound anæmia which may last for a long time without any discoverable lesion of an mportant viscus to account for it.

DIAGNOSIS.—It may be said that before the rash has appeared it is impossible to make a positive diagnosis of scarlet fever, since at this time there are no characteristic symptoms, such as occur in measles. During an epidemic if a child is seen who has been vomiting and has a high temperature with catarrh of the pharynx, it may be strongly conjectured that the patient is suffering from scarlet fever, but the physician will be wise not to commit himself positively to such an opinion. As a rule, since the period of invasion is so short, the physician will not see the case till the eruption has appeared. Generally when the rash has become fully developed the diagnosis offers little difficulty. The height of the fever, the evident illness of the patient, the character of the rash and the positions which it first occupies upon the body, the sore throat, the enlargement of the ganglia at the angles of the jaws, and the presence in the urine of a trace of albumin will declare the nature of the disease. In the malignant cases where death occurs before the eruption comes out the diagnosis can be made only by considering the height of the fever, the nervous phenomena, and the fact of the existence of an epidemic or history of exposure, with the possibility of excluding other causes for the same train of symptoms. The chief difficulties in diagnosis will often arise in connection with those cases which present irregularities in their course. In all such cases a point of the very highest diagnostic value will be to establish the probability of infection. In those rare cases which run their course without fever, to which reference has been made, one will have the greatest difficulty in arriving at a diagnosis of scarlet fever, for a rise in temperature is so essentially connected with our ideas of scarlet fever that its absence will always throw doubt on the diagnosis. If in addition to a characteristic rash there were sore throat and albumin in the urine, the presumption would be in favor of scarlatina, and this would be much strengthened should lamellar desquamation or nephritis develop at the usual time; and especially would the supposition be confirmed should an ordinary case of scarlet fever occur after exposure to infection from the anomalous case.

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[1] *Wiener medicinische Blätter*, B. 15, H. 28.

In view of the likelihood that scarlatina may occur without any eruption, it seems to the writer that during an epidemic all cases of sore throat, especially where albumin is present in the urine, should be regarded with suspicion, and if possible treated as though they were cases of scarlatina. This will no doubt be a difficult and often a thankless task, but in our present state of knowledge a due regard for the public safety dictates such a course, more especially as the sore throats which occur during an epidemic of scarlatina are infections whether they be scarlatinal or not.

The cases of scarlatina in which the nervous symptoms are such as to cause a resemblance to cerebro-spinal meningitis can usually be distinguished from the latter affection by the facts that in scarlet fever there is an inflammation of the throat, while in meningitis the rash most often presents itself in the form of petechiæ.

When seen after the first stages of the illness have passed away the typhoid form of scarlatina might be mistaken for typhoid fever, but the history of the onset, and perhaps the presence of desquamation, would help to distinguish the two maladies.

Those cases in which the rash comes out first in some unusual site need not create confusion, as in a short time, under ordinary circumstances, the eruption extends all over the body, when the usual picture of scarlatina is presented. More difficulty is experienced in coming to a conclusion where the rash occupies only limited portions of the surface, for the disease is apt to be mistaken for an erythema. In scarlatina there are fever, sore throat, strawberry tongue, albumin in the urine, and when desquamation occurs it affects not only the portions of the skin which have been involved in the eruption, but also those parts which were free from the rash. This combination of phenomena could hardly occur with an erythema.

Especially in cases where the rash of scarlet fever remains discrete the disease may be confounded with measles or rötheln. In measles the incubation period is much longer than in scarlatina: the invasion period of measles occupies four days with well marked catarrhal symptoms, but lacks the sore throat, the high fever, the vomiting, and the nervous phenomena of scarlet fever, while albumin is absent from the urine. The eruption of measles is maculo-papular and of a duskier hue than the rash of scarlatina; the borders of the lesions of measles are crenated, and they are often collected into crescentic groups, while the whole face is affected by the eruption, the region about the mouth not being avoided, as is the case in scarlatina; the rash of measles stays out on the body in full bloom a shorter time than the eruption of scarlet fever. The desquamation of measles occurs as furfuraceous scales, while in scarlatina large lamellæ are usually thrown off. Finally, the complications and sequelæ of the two diseases are entirely different.

In rötheln the period of incubation is much longer than in scarlet fever. Rötheln often has no invasion stage, the first evidence of the disease being the rash, and if there are premonitory symptoms they are not so severe as those seen in the invasion of scarlatina. The rash of rötheln occurs as round rose-red spots, with well defined borders; it most resembles scarlatina when it becomes confluent, but this generally occurs only in patches, and these lack the color and punctate appearance usually presented by the eruption of scarlatina; and, furthermore, rötheln affects the region about the mouth. In rötheln there is sore throat, but it is generally not so intense as the angina of scarlet fever. In rötheln there is slight fever, and the patient is often not at all ill, but the opposite is true for scarlatina. The tongue of scarlet fever is characteristic, that of rötheln is only coated. The urine of rötheln is at most febrile urine, while in scarlatina the urine contains albumin and casts. In rötheln the glands along the course of the sterno-mastoid are involved; in scarlet fever those at the angles of the jaws, and, moreover, the degree of enlargement of the glands has a more constant relation to the condition of the throat in scarlet fever than is noticed in rötheln. After rötheln desquamation is rare, and the disease has no special complications or sequelæ.

There is no likelihood of confounding scarlatina with smallpox after the true eruption of the latter disease has appeared, but there are certain pre-eruptive erythemas with smallpox which might lead to confusion. Smallpox, when the eruptions referred to are apt to appear, is characterized by severe lumbar pains and intense headache, while there is no sore throat nor the peculiar tongue of scarlatina. The erythematous rashes of smallpox usually occur in certain regions, especially the triangle of Simon and the pectoral triangle, and are very prone to exhibit a petechial character.

Accompanying epidemics of influenza rashes have been observed which might cause the affection to be mistaken for scarlet fever. In influenza there is usually severe aching pain in the back and limbs; the throat is sore, but generally the angina is not so intense as that seen with scarlatina; in influenza there is commonly a bronchitis or other involvement of the lung. The rash of influenza partakes more of the character of measles than of scarlet fever, usually occurring as small, discrete red macules.[1] The rash of influenza is more evanescent and irregular than that of scarlatina, often going and returning several times during the course of the malady.

Erysipelas could hardly be mistaken for scarlet fever. The rash of erysipelas is limited to a region of the body, often develops around a wound, and does not present the punctate redness seen in scarlatina. There is also more hyperæsthesia of the affected area and more œdema of the subcutaneous tissue than is observed with scarlet fever, while desquamation in erysipelas is confined to the region which has been involved by the eruption.

There are a large number of drugs which ingested cause an eruption resembling that of scarlatina. The more important are here mentioned: benzoic acid, boracic acid, salicylic acid, antipyrine, arsenic, belladonna, chloral, chloralamide, chloroform (inhaled), digitalis, mercury, hyoscyamus, iodine compounds, opium preparations, phenacetin, tar, quinine, rhubarb, stramonium, strychnine, sulphonal, tuberculin. The above list includes only a small number of the drugs which at one time or another have been observed to be followed by a rash more or less resembling scarlatina. It is to be noted that many substances when applied to the skin are capable of causing a scarlatiniform erythema, as mustard for instance. Specially are certain substances used in modern antiseptic surgery capable of causing such an eruption. Among these may be mentioned carbolic acid, iodoform, and bichloride of mercury. Generally the rashes caused by the application of these drugs are local in character, but often they have become generalized. Recent French literature presents quite a number of instances of generalized scarlatiniform eruptions following the use of mercury as a local application.

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[1] Hardaway, oral communications.

The diagnosis of these drug eruptions from scarlatina will be most easily made by first ascertaining the fact of administration of a drug capable of exciting a scarlatiniform rash; then the facts that the drug eruption is not preceded by the prodromata of scarlet fever, and that it is not accompanied by the sore throat, high fever, strawberry tongue, and enlargement of the lymphatic ganglia. In cases where the history cannot be obtained it should be remembered that some of these drugs produce symptoms peculiar to themselves, which are not apt to be found with scarlatina, as with digitalis the slowing of the heart, with belladonna the dilatation of the pupils, salivation with mercury, contracted pupil and drowsiness of opium, pruritus and heightened reflexes with strychnine, and the peculiar odor which some drugs impart to the breath or urine, as chloroform or turpentine. A further point of assistance will be the fact that upon the withdrawal of the drug the rash generally subsides more rapidly than would the rash of scarlatina. The difficulty of differential diagnosis is increased by the fact that in some rare cases—as, for instance, has been observed with chloral—there may be with the drug eruption, fever, and a subsequent desquamation.

There is a dermatosis which very closely simulates scarlet fever, so nearly indeed that it is called erythema scarlatiniforme. It is not a distinct and separate disease, but occurs as a concomitant of other diseases. It is of special frequency in such septicæmic conditions as follow surgical wounds and the puerperal state. In speaking of wound scarlatina reference has been made to this. This eruption occurs with other diseases also, as gonorrhœa, diphtheria, typhoid fever, rheumatism, ague, uræmia, and it has been induced by certain foods, as shellfish and various fruits. It may at times be impossible to differentiate this dermatosis from irregular forms of scarlatina. The following points will assist in the diagnosis: In scarlatiniform erythema the throat is not so severely inflamed as in scarlet fever, nor is there the strawberry tongue, and the constitutional symptoms are lighter. The demonstration of albumin and casts in the urine would speak strongly in favor of scarlet fever, except in those cases where erythema scarlatiniforme complicates a disease prone to be accompanied by nephritis. In erythema scarlatiniforme desquamation usually begins on the third or fourth day, while in scarlet fever it most often occurs at a much later date. Finally, erythema scarlatiniforme is apt to occur in repeated attacks.

In rötheln the period of incubation is much longer than in scarlet er. Rötheln often has no invasion stage, the first evidence of the ease being the rash, and if there are premonitory symptoms they are so severe as those seen in the invasion of scarlatina. The rash of ln occurs as round rose-red spots, with well defined borders; it resembles scarlatina when it becomes confluent, but this generally rs only in patches, and these lack the color and punctate appearance lly presented by the eruption of scarlatina; and, furthermore, rötheln ts the region about the mouth. In rötheln there is sore throat, but generally not so intense as the angina of scarlet fever. In rötheln re is slight fever, and the patient is often not at all ill, but the opposite rue for scarlatina. The tongue of scarlet fever is characteristic, that ötheln is only coated. The urine of rötheln is at most febrile urine, ile in scarlatina the urine contains albumin and casts. In rötheln glands along the course of the sterno-mastoid are involved; in scar- fever those at the angles of the jaws, and, moreover, the degree of nlargement of the glands has a more constant relation to the condition of the throat in scarlet fever than is noticed in rötheln. After rötheln desquamation is rare, and the disease has no special complications or sequelæ.

There is no likelihood of confounding scarlatina with smallpox after the true eruption of the latter disease has appeared, but there are certain pre-eruptive erythemas with smallpox which might lead to confusion. Smallpox, when the eruptions referred to are apt to appear, is characterized by severe lumbar pains and intense headache, while there is no sore throat nor the peculiar tongue of scarlatina. The erythematous rashes of smallpox usually occur in certain regions, especially the triangle of Simon and the pectoral triangle, and are very prone to exhibit a petechial character.

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y been mentioned that serious intracranial mischief may result suppurative otitis media. Whether or not affections of the eye o the gravity of the prognosis will depend on the nature of the mplication. A simple conjunctivitis would not be regarded as of import, while a panophthalmitis would increase the gravity of ase. In general, it may be said that any complication renders the nosis unfavorable in proportion to the importance of the organ lved and the severity of the involvement.

REATMENT.—It is convenient to consider the treatment of scarla- ler three heads—prophylaxis, hygiene, and therapeutics.

laxis.—By far the most important part of the treatment of et fever in our present state of knowledge consists in prophylaxis. n this standpoint treatment aims at the prevention of scarlatina the limitation of its spr as far as may be, when it has occurred. s far, there is no remedy own which has the power of destroying susceptibility to the disease. Prevention must therefore, for the resent, interest itself in closing as far as possible those avenues by which the poison is brought into contact with susceptible persons. This will include, in the first place, a careful supervision on the part of health boards of the health of all individuals who are brought into close contact with their fellows. There can be no doubt that scarlet fever is often acquired by school children from mild cases of scarlatina which have occurred in the school and passed unnoticed or have been regarded as some simple rash. Furthermore, children often are allowed to return to school too soon after an attack of scarlatina and without a proper disinfection of their clothing, books, etc.

The progress of preventive medicine in its relation to scarlatina would no doubt be much furthered were thoroughly equipped hospitals established in all cities where those affected could be at once isolated and properly cared for. Where cases are treated at their homes it may be said that, as a rule, complete isolation is impossible.

So many facts point to the possibility of carrying the scarlatinal poison in milk that special attention should be directed to the milk supply of all communities. Not only should no dairyman in whose family a case of scarlet fever exists be allowed to distribute milk until thorough disinfection has been carried out, but all herds of milch cows should be inspected from time to time, and those with vesicular eruptions of the udder or desquamating patches upon the body should be isolated and their milk not used.

When a case of scarlatina occurs in a family, it is of the highest importance for the sake of the unaffected to isolate the case at once. The apartment chosen as the sick chamber should be at the top of the house, and the well children should be kept in the lower story, as by this means all communication between the sick and the well is as far as possible interrupted. From the sick chamber should be removed all objects except such as are needed in the proper nursing of the case. Thus all pictures, carpets, hangings, curtains, upholstered furniture, and bric-à-brac should be banished. No one should have access to the room save the physician and nurse. Over the door of the chamber should be hung a sheet kept wet with a 5 per cent. solution of carbolic acid. It is of the highest importance to see that no object of any description is allowed to leave the room until it has been thoroughly disinfected. Any food remaining from the meals of the patient or nurse should be either destroyed in the room or immersed for some hours in a bucket filled with a 10 per cent. solution of carbolic acid before being carried out. The urine and fæces of the patient are to be placed for some time in a similar solution before they are removed. For the purpose of cleansing the throat and nose of the patient soft rags are to be recommended, which should then be burnt in the fireplace in the room. When the clothing of the patient is changed, before that which is removed is put in the laundry it should be boiled for an hour in a 5 per cent. solution of carbolic acid or a 1 : 1000 solution of bichloride of mercury. The nurse should wear a washable dress, and before going into the presence of those susceptible should carefully cleanse her person in the same manner soon to be recommended for physicians, and change to a fresh dress. It is not a good plan to allow a cat or a dog to remain in the chamber for the amusement of the sick child, as it has been shown that in some cases scarlet fever has been carried by such animals to those who are well. The physician, who has necessarily to mingle with susceptible persons after leaving a scarlet fever case, should neglect no precaution to avoid carrying the infection. It is an excellent plan to wear a light rubber coat during the visit. This can be wiped off with a sponge dipped in an antiseptic solution after leaving the sick room, and thus the clothing is prevented from conveying the infection. The hair could be in a manner prevented from absorbing the virus by wearing during the visit a silk or rubber cap, which should be removed on leaving the room. On arriving at his home the physician should adopt the further precaution of removing the suit which he has worn during the call; this clothing should be hung in a well ventilated room in the sunlight for a few days before it is again worn. Before calling on another patient the hands and face should be washed, using some good antiseptic soap, such as Eichhoff's menthol-eucalyptol soap.

During the whole course of the disease a dish of water into which carbolic acid or eucalyptus oil has been placed should be kept boiling over a lamp. This may have some influence in limiting the diffusion of the scarlatinal virus.

The patient should remain in the sick room till desquamation is entirely completed. The chamber and all that it contains must then be carefully disinfected. All articles which can be spared should be destroyed by burning. Objects which cannot be spared can be disinfected in several ways. For such as will not be injured by the process the best method of sterilization is by steam under pressure. This method is especially suitable for bedding and clothing. For its application somewhat elaborate apparatus is required, which will generally limit the use of this process to those municipalities which have provided proper disinfecting stations. In lieu of steam all articles, as far as possible, should be boiled for an hour in the carbolic or mercuric solution mentioned above. For objects which cannot be thus sterilized some one of the gaseous disinfectants must be used. Perhaps one that is as good as any other, while at the same time it is easy of application, is the liberation in the room of sulphurous acid vapors. In order to be most effective steam should be liberated in the room at the same time that phur is burnt, since sulphurous acid is most active in the presence of moisture. At least 3 pounds of sulphur for every 1000 cubic feet of oom space must be burnt. The sulphur candles now obtainable in all ug stores are convenient, or the sulphur may be finely broken and xed with alcohol to secure its thorough combustion. It is burnt in iron pan placed upon bricks in a tub of water to prevent danger n fire. Previous to liberating the gas all cracks around windows nd doors should be stopped with paper and the room rendered as tight s possible. The gas should be left in the room for a day at least. he paper upon the walls of the chamber should be removed and fresh paper applied, or, where paper is not used, the walls should be wiped down with bichloride solution and then freshly lime-washed. The floor should be scrubbed with soap and water and then freely washed with bichloride solution. All the furniture in the room must be washed with the solution, and it is an excellent precaution to have it revarnished. All books and toys which have been used by the patient should be destroyed by burning, as such articles are very difficult to disinfect.

It may seem that all these precautions are difficult to carry out, and many have urged against them that even when they are carefully observed scarlatina may be contracted by other members of the family. Statistics, however, show that with thorough enforcement of these measures the disease is less apt to be conveyed, and it is manifestly the duty of the physician to enforce anything that offers a reasonable hope of checking the spread of so formidable a malady as scarlatina.

Hygiene.—The hygienic surroundings of the patient must be made as good as possible. The sick room should be a large chamber with abundant means for ensuring thorough ventilation. Usually this can best be accomplished by having an open fire burning in the grate. There should be maintained an even temperature of 70° or 75° F. The linen of the patient and of the bed should be kept fresh and clean. The bedclothing must be warm but light.

It is wise to endeavor to keep the skin in good condition, as we often have to depend upon its activity to accomplish the work of a damaged kidney. To this end a full warm bath should be given each evening, and if the fever is high this will be still more necessary. After the bath the surface should be anointed with a bland fatty substance which has an antiseptic property. This gives ease to the swollen, tender skin, often reduces the temperature, and is supposed by many to prevent the volatilization of the scarlatinal poison. A good formula for such an ointment is—

R.	Acidi carbolici,	♏iv ;
	Olei eucalypti,	♏xx ;
	Vaselini,	ʒvj ;
	Unguenti aquæ rosæ,	ʒij.—M.

The careful antiseptic treatment of the throat forms an important part of the hygienic management, but it will be considered later on.

Jamieson believes that desquamation can be accelerated, while at the same time the scales are rendered less infectious, by a daily bath with Eichhoff's resorcin-salicylic soap. The lather from this soap is to be well rubbed in with a piece of flannel, and then the surface washed with warm water. In the case of the palms and soles the soap should be used several times a day. Each use of this soap upon the body should be followed with inunction of the ointment recommended above.

The length of time which must be spent in the sick room is a question concerning which there is a variety of opinion. The only safe rule is that the patient must remain isolated till desquamation is entirely completed. In the opinion of the writer it is the wisest plan to confine the patient strictly to bed till desquamation is finished. Reference has already been made to the injurious effects of exposure of the surface to varying degrees of temperature, and of the erect posture. Both of these evil influences are best avoided by a sufficiently long stay in bed.

The diet of the person suffering from scarlet fever should be light, but nutritious. Milk forms the ideal food in a large proportion of the cases. Where it is not readily taken in its simple form, some one of its preparations may be substituted, as, for instance, koumyss, kefyr, or peptonized milk. Often the addition of lime water renders the milk more digestible. In older patients the diet may occasionally be varied by allowing a soft-boiled egg, or oysters raw or stewed with crackers or toast. The patient ought to be fed at frequent intervals, and only small amounts given at a time, as very often the digestive processes are so impaired as to render the proper preparation and assimilation of any but small quantities of food impossible. Under such circumstances systematic stuffing of the patient can be only injurious, as a large amount of material is introduced which will not be taken up by the tissues, but must be removed from the body partly by the kidneys, which are already incapable of their normal amount of work. In some cases the stomach is so irritable that it cannot be made to retain food; when this is the case rectal alimentation must be used, though this form of feeding is not so well borne by children as by adults. Water both in its ordinary form and carbonated alkaline waters should be allowed as freely as the patient desires.

Therapeutics.—From time to time many remedies have been vaunted as specifics in the treatment of scarlatina. It is hardly necessary to refer to belladonna, which has enjoyed a reputation with some, apparently for no better reason than the fallacious one that because it can produce a rash like scarlet fever it can also prevent or cure the disease. Illingworth claims that biniodide of mercury is a specific, and Duke says it arrests fever and prevents desquamation. Shakhovsky lauds salicylic acid as being capable of preventing all complications and of arresting them when present. A wide experience with any or all of these remedies will probably convince the practitioner that their apparent specific action depends more on the mildness of the epidemic than the curative nature of the drug.

The milder forms of the disease demand little in the way of internal medication. The diet and hygiene should be arranged in accordance with the principles already set forth. The author has for many years made it a rule to administer to nearly all cases of scarlatina iodide of potassium and bichloride of mercury. It has seemed to him that these drugs at least modify the severity of the symptoms and o r a child three years of age the iodide of potassium may be given in following prescription :

℞. Potassii iodidi, gr. xlviii ;
Syrupi limonis, ℥j ;
Aquam, ad ℥iij.—M.
Sig. A teaspoonful three times a day in water.

The bichloride is most elegantly administered in the form of Van vieten's liquid. To a child of three a third of a teaspoonful should given in water three times a day.

It has been the custom for a long time to administer in scarlet fever tincture of the chloride of iron. For this drug it is claimed that it is of use in counteracting the acute anæmia which often exists, that the chlorine it contains has a valuable antiseptic action, and that the local effect upon the throat as the medicine is swallowed is beneficial. The iron is often combined with chlorate of potash, as in this prescription :

℞. Potassii chloratis, ʒj ;
Tincturæ ferri chloridi, ʒiss ;
Syrupi, q. s. ad ℥ij.—M.
Sig. Half teaspoonful every three hours for a child three years old.

Wilson of Philadelphia has recommended the administration of chloral throughout the whole course of the disease. He claims that by this means the nervous symptoms are controlled and the condition of the patient is rendered more comfortable. The drug is to be given in small doses at repeated intervals, and any deep narcotism is to be avoided, but the patient is to be kept in such a condition that though easily aroused he soon falls asleep again. Wilson recommends the following manner of administration :

℞. Chloralis, gr. xxx ;
Syrupi lactucarii (Aubergier),
Aquæ, āā. ℥j.—M.
Sig. Teaspoonful as often as necessary for a child of three.

The condition of the bowels should receive attention. When constipation exists a mild aperient or an enema should be given. The importance of preventing constipation would assume much importance could we accept Mahomed's opinion as to the frequent causal relation of this condition to nephritis.

No part of the treatment of scarlatina is more important than the local treatment of the throat and nose. By proper care of these regions not only may the severe throat complications often be prevented, but ear trouble can usually be averted.[1] An ice bag applied over the neck tends to subdue the faucial inflammation and at the same time often lowers the temperature. Swallowing of small bits of ice at frequent intervals exerts a beneficial influence, as is often evinced by the lessened pain on deglutition. Some antiseptic wash should be used in the nose and throat as often as possible. It not infrequently happens that there is such turgescence and swelling of the inferior turbinated body as to hinder the free access of the antiseptic to the posterior nares. This can usually be overcome by applying to the turbinated body with a cotton swab a 4 per cent. solution of cocaine. In older children and adults the antiseptic solution may be applied by a spray apparatus or nasal douche, but in young children it is often necessary to use a dropping tube for this purpose. A great number of antiseptic fluids have been suggested, but perhaps none is better than a 2 or 3 per cent. solution of boric acid. Six to ten drachms of this, warmed to the temperature of the body, should be used in the nasal cavities two or three times a day. When a spray apparatus can be used the throat should also be sprayed with the same solution. If the throat symptoms are mild, this alone suffices, but when the inflammation is intense great good is derived from the thorough application with the cotton holder of a 10 per cent. alcoholic solution of salicylic acid. This should be used once or twice a day. After the use of all these applications it is well to apply both to the nose and throat an antiseptic oil. This can be used in a spray, or a few drops may be introduced into the nose, whence they will run back into the throat. A good formula for such an oil is—

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[1] Spencer, oral communication.

℞. Camphoræ,
Menthol, *āā.* gr. iij;
Albolene, ℥j.—M.

In the case of individuals who can gargle it is of advantage to use an antiseptic solution for this purpose at frequent intervals. According to Yeo, one of the best preparations to be thus used is chlorine water made in the following way: Into a sixteen-ounce flask put eight grains of chlorate of potash. Upon this pour one drachm of hydrochloric acid. When the green vapor has filled the bottle pour in water little by little, corking and shaking after each addition, till the bottle is full. This not only makes an excellent local application, but by many is prized as an internal remedy, a teaspoonful or two being swallowed every two hours. Another prescription which is frequently used by the writer as a gargle and also as a spray is—

℞. Acidi carbolici, ʒss;
Glycerini, ʒv;
Sol. pot. chloratis sat., q. s. ad ℥v.—M.
Sig. Dilute at time of use with equal parts of warm water.

The treatment outlined above is sufficient for the ordinary cases of scarlet fever. Since any additional treatment will depend on the severity of the particular symptoms presented by each case, it will facilitate matters to discuss the treatment of some of the more important symptoms which are likely to arise.

One of the chief symptoms which the physician is called upon to combat is fever. As long as the temperature remains below 103° F., it does not constitute a dangerous condition unless it be unduly prolonged.

For the reduction of temperature the use of drugs is not, as a rule, to be so highly recommended as the abstraction of heat by means of the application to the body of cold. Quinine is a drug which has some antipyretic action, and used in reasonable doses it also acts as a tonic. One half to three grains, according to age, given every two hours, may be considered as expressing the limits of the usual dose for children. Quinine, according to Yeo, if given dissolved in the chlorine water mentioned above, will have a more decided effect in lowering temperature than if given in powder or capsules. It seems also to exert a more decided action when given in an effervescing mixture. The formula for the alkaline portion of the mixture is—

℞. Sodii bicarbonatis,	gr. xx ;
Potassii bicarbonatis,	ʒss ;
Potassii chloratis,	gr. vj ;
Aquam,	ad ℥jv.—M.

The formula for the acid part is as follows :

℞. Quininæ sulphatis,	gr. viij ;
Acidi citrici,	gr. xx ;
Syrupi limonis,	ʒiij ;
Aquam,	ad ℥iv.—M.

From a dessertspoonful to a tablespoonful of each portion of this prescription is mixed together at the time of administration.

The drugs which have the greatest potency in reducing temperature are the coal-tar derivatives. The best known of these are antipyrine, phenacetin, and acetanilid. It may be said that all of these preparations are dangerous on account of their depressing effect, and if given should be used with caution, especially in a disease like scarlet fever, where the vital powers are already below par. Phenacetin is the safest of these drugs, and it has the advantage that its sedative effects are quite marked. If administered, it is best given in small doses at frequent intervals, for the effect desired can be thus more exactly obtained than if large doses are exhibited.

By far the best and safest manner of controlling the temperature is by direct abstraction of heat from the body. There are a number of methods by which this can be accomplished. A simple means is to apply bags of ice to portions of the body where a considerable volume of blood is flowing close beneath the surface, as over the neck and wrists. In this way a marked reduction of temperature can often be effected. A more prompt effect is produced by sponging the whole body with cool water or equal parts of water and alcohol. To be of avail the sponging must be repeated at frequent intervals. The cold pack is an efficient method of reducing fever, but one that it is often impossible to use on account of the prejudices of the parents or friends of the patient. In practice the cold pack is thus applied : A blanket is spread upon a cot ; over this a sheet wrung out of water at a temperature of 70° F. is placed. The patient is enveloped, with the exception of his head, in the sheet, and the blanket is wrapped over all. When a sufficient reduction of temperature has been secured, the patient is removed from the pack and wrapped in a dry, warm blanket. The most powerful as well as the most certain method of rapidly lowering the temperature is the full cool bath. A bathtub large enough to admit of the patient's lying at length is filled with sufficient water at a temperature of about 100° F. to cover the body. After the patient is placed in the tub the bath is gradually cooled, by the addition of cold water, to a temperature of 80° or 75° F. While the patient is in the bath the effect may be still further increased by applying to the head an ice cap. The length of time that the bath is continued will vary with the effect produced, but it is a good rule to remove the patient before the temperature reaches the normal, as not uncommonly it continues to fall for some time after leaving the bath. While the bath is being administered a careful watch should be maintained upon the patient, and any cyanosis or lividity, or weakness or irregularity of the pulse, or complaint of chilliness, should be the signal for the cessation of the bath. A warm blanket should be ready to receive the patient, and after his surface has been rapidly dried he should be tucked snugly in bed. If prostration follows, as occasionally will happen, alcoholic stimulants must be administered.

The treatment of the unpleasant or dangerous symptoms on the part of the nervous system will vary according to their character. Great restlessness and active delirium are usually best controlled by the bromides of soda or potash. Sometimes a combination of bromides with chloral is very efficient. It is well, especially in cases where there is marked rapidity of the pulse, to add to the mixture digitalis, as in this prescription:

℞. Chloralis,	gr.xlviij;
Potassii bromidi,	ʒj;
Tincturæ digitalis,	♏xvj;
Syrupi pruni Virginianæ,	ʒv;
Aquam,	ad ℥ij.—M.

Sig.—One half to one teaspoonful every two hours for a child three years old.

Convulsions in the early stages of the disease can usually be controlled by the same drugs, but it will often be necessary to administer them *per rectum*. In addition, it is frequently of the greatest benefit to immerse the whole body in a warm bath. At a later period of scarlet fever convulsions generally depend on the presence of some complication, and the treatment will be largely that of the complication. When the nervous manifestations are accompanied by high fever a reduction of the temperature will usually produce an amelioration of these symptoms. In cases where a low form of delirium exists or the patient is in a semi-comatose condition, with rapid, weak pulse, as occurs in the malignant forms of scarlatina, thorough and systematic stimulation will from the first be necessary. As stimulants the alcoholic preparations, such as brandy or whiskey or sherry wine, rank first. The amount of alcohol which can be given varies with the age of the patient and his susceptibility to the remedy. It is often of importance to add full doses of digitalis to the alcohol. Thus for a child of three years one may order—

℞. Tincturæ digitalis, ♏xl;
Spiritus frumenti, ℥iij.—M.
Sig. Teaspoonful every two hours.

It is well to give this in milk, as we can thus stimulate and nourish at the same time. Carbonate of ammonia may also be used as a stimulant, or equal parts of spiritus ætheris compositus and spiritus ammoniæ aromaticus with camphor water may be administered, or in urgent cases camphor dissolved in olive oil may be given hypodermically. In the opinion of the writer these measures are not so reliable nor of such universal application as the whiskey and digitalis mixture recommended.

Occasionally diarrhœa and vomiting are so persistent as to require special treatment. Vomiting may usually be stopped by the application over the stomach of a mustard or spice poultice, while small bits of ice are swallowed at frequent intervals. When this does not suffice the administration of champagne in very small, frequently repeated doses will often prove of benefit. It may be necessary in severe cases to resort to some of the numerous stomachic sedatives. A useful prescription is—

℞. Cocainæ hydrochloratis, gr. 1/6;
Acidi carbolici, ♏v;
Aquæ laurocerasi, ʒv;
Aquam, ad ℥ij.—M.
Sig. Teaspoonful every hour.

For diarrhœa quite often the application of cold compresses over the belly will suffice. Internally such a powder as the following may be administered:

℞. Bismuthi subcarbonatis, ʒss;
Pulveris ipecacuanhæ compositi, gr. v.—M.
Fiant pulveres, No. x.
Sig. One every two hours for a child three years old.

To treat appropriately the complications and sequelæ of scarlet fever will often demand all the skill of even the most accomplished physician. Here only the treatment of the more important and most common of these conditions can be considered.

The treatment of the throat inflammation as it is seen in the ordinary cases of scarlatina has been sufficiently dealt with, and it only remains to make some suggestions as to the treatment of the severer forms of angina. In cases where there is a false membrane or slough the throat should be first cleansed by means of a spray of peroxide of hydrogen, and then one of the antiseptic solutions recommended above should be used. There are many who make use of a 1 : 500 or 1 : 1000 solution of bichloride of mercury applied to the throat on a cotton swab after the pharynx has been cleansed with the peroxide. When there is cellulitis of the neck an ice bag should be constantly applied. As soon as it can be determined that pus has formed an opening must be made under antiseptic precautions, and thorough drainage for the abscess provided. The treatment of diphtheria complicating, scarlatina does not differ from the treatment of the malady when occurring alone. Today it seems that Behring's "heil-serum" is in a fair way to banish the multitudinous drugs which have been used in the treatment of this complication. In all the forms of severe throat complications early and systematic stimulation is of the utmost importance. It sometimes happens that on account of the pain of swallowing there is difficulty in persuading the patient to take a sufficient quantity of nourishment. Under such circumstances cold, liquid food is most suitable, but it may be necessary to give nourishment *per rectum.*

If careful and systematic cleansing and disinfection of the nose and throat is practised, the number of cases in which middle-ear inflammation arises will be comparatively small, but the physician should always be on the alert for the first evidence of this important complication. As a rule, the patient complains of pain in the ear, but if the mental faculties are blunted or if the patient is a very young child, such notice of otitis may not be given. It is therefore a wise plan for the physician during the height of the disease daily to inspect the ear with head mirror and speculum. In the early stages of the ear trouble the pain is usually due to closure of the Eustachian tube, and inflation by Politzer's method may afford great relief. In addition to this, chloroform vapor may be applied to the ear by placing in a good sized wine-glass, previously warmed by immersion in hot water, a few drops of chloroform on a piece of cotton; the glass is then pressed closely over the ear. Another application which at this time often gives relief is a small bag filled with salt or bran well heated and placed on the ear. A leech placed behind the ear will often prove of great benefit. When inflammatory secretions have accumulated in the ear in sufficient quantity, severe pain is caused by the tension thus produced. This condition can be relieved only by spontaneous rupture of the drumhead or by surgical art. When the drumhead is found reddened, tense, and bulging, an opening in it should be made. By this means an escape of the imprisoned fluids with cessation of pain is secured, and damage to the delicate structures of the ear as well as the tedious recovery which follows a spontaneous rupture is avoided. The opening should be made at the most prominent portion of the membrana tympani with a cataract needle, special care being used not to thrust the needle deeper than is necessary to perforate the membrane, thus avoiding injury to the chorda tympani or other important structure. If suppuration of the ear with perforation of the drumhead has occurred, the external auditory canal should be gently syringed twice a day with an antiseptic solution, such as a 2 per cent. boric acid or a 1:5000 mercuric bichloride solution. The orifice of the meatus should be kept closed with an absorbent cotton plug. For an account of the treatment of other serious ear complications the reader must be referred to special treatises on diseases of the ear.

In those cases of scarlatina in which conjunctivitis occurs the eye must receive special attention. The room in which the patient lies hould be shielded from too great a glare of light. By anointing with aseline or unguentum aquæ rosæ agglutination of the eyelids is pre-ented, and thus the comfort of the patient is increased. Several mes a day cloths wet in the following solution should be placed over eyes for ten or fifteen minutes at a time:

℞. Acidi borici, ʒss;
Tincturæ opii deodoratæ, ʒiv;
Aquam, ad ℥iv.—M.

When keratitis is present, cloths wrung out of boric acid solution as hot as can be comfortably borne should be kept on the eyes. When sloughing of the cornea results, panophthalmitis with loss of the eye follows. Paralysis of the muscles of the eye following scarlet fever requires such treatment as is applicable under similar circumstances in other regions of the body.

Bronchitis and catarrhal pneumonia complicating scarlet fever demand the same treatment which would be appropriate under other circumstances—stimulating and supportive measures, proper protection of the chest, and hydrotherapy.

Attention has been called to the frequency with which pleuritis arising during scarlet fever is purulent. This suggests a prompt use of the aspirator in pleural effusions, and especially as the physical signs of fluid in the chest in young children are often equivocal. If pus is found, provision must be made for draining the chest. In children repeated aspiration is more apt to succeed than is the same procedure in adults, but even in children this method cannot be relied upon, and if the condition of the patient will permit it is better to open the chest, resecting a rib if necessary. A drainage tube must be introduced of such a size and in such a position as to secure thorough drainage. In every case of empyema careful stimulation and nutrition is of the highest importance.

Pericarditis and endocarditis require the use of digitalis to slow and strengthen the pulse. In the earlier stages of both affections an ice bag should be kept over the heart. If fluid accumulate about the heart in sufficient quantity to impede its action, it must be removed by aspiration. In pericarditis the outlook is especially unfavorable, since the condition of the patient does not offer encouragement for undertaking those serious surgical procedures which are necessary for draining the pericardium of a purulent accumulation.

Scarlatinal rheumatism is usually so mild as not to need any special treatment, or at most the application of an anodyne liniment, such as the chloroform liniment, with a layer of cotton wool held in place by a firmly adjusted bandage. In severe cases the salicylate of soda and an opiate may be necessary. When a suppurative synovitis occurs the condition demands surgical interference, which is often rendered of no avail by the pyæmic condition of the patient.

The proper treatment of scarlatinal nephritis demands the most careful consideration. Attention has been called to the prophylactic treatment of this complication. If this part of the treatment is properly carried out, the cases of dangerous nephritis will be comparatively rare. The danger to life in nephritis arises chiefly from two causes—the failure of the elimination of waste products from the body by the kidney, and the accumulation in the cavities of the body of serous fluids. To prevent both of these contingencies it is necessary to bring into active play the accessory emunctories of the body, the skin and intestinal canal, as well as to encourage as thorough functioning of the kidneys as may be possible. When the urine is only slightly decreased in volume with a fairly normal amount of solids in solution, a rather warm temperature of the sick chamber, clothing of the patient in flannel, a fluid diet, and regulation of the bowels will be all the treatment required. If under these measures the condition does not improve, but, on the other hand, the urine grows scantier or less solids are eliminated, the full activity of the skin should be called to the assistance of the kidneys. The activity of the skin may be stimulated by hot water, hot air, or steam, or by the administration of drugs. Very often the most convenient way of provoking diaphoresis will be the hot bath. The patient is immersed in water at a temperature of 90° F., and the heat of the water is gradually raised to 105° or even 110° F. The duration of the bath should be from fifteen to twenty minutes. At the close of the bath the patient should be rapidly removed to a warmed bed and covered with several blankets. If perspiration follows, the bath has been of use, and may be repeated two or three times a day according to the urgency of the case. If no perspiration follows, one of the other methods of promoting diaphoresis must be tried. For instance, after the patient has been removed from the hot bath the effect may be kept up by surrounding his body with bottles filled with hot water. At times a steam or hot air bath succeeds where the ordinary hot bath has failed. A steam bath may be administered by placing over the patient blankets elevated slightly above the body by a frame, so as to form a sort of canopy; the ends and edges of the blankets are tucked carefully around the patient, only his head being left out, so that when the steam is introduced under the blankets it will not escape. By means of a rubber tube steam is conveyed from a suitable generator, such as a croup-kettle, and passed under the blankets, where it surrounds the body in a hot vapor bath. The same thing may be accomplished by placing around the patient hot bricks wrapped in wet cloths and covering snugly with blankets. The hot air bath can be given by causing the patient to sit on a chair with a blanket fastened around the neck and coming down to the floor all around; under the chair a small quantity of alcohol is burned upon a plate. If the condition of the patient does not permit his sitting up, a hot air bath may be conveniently given by placing around him while in bed several Japanese stoves and covering with blankets. The effect of any one of these methods may be still further increased by administering at the conclusion of the bath a hot drink, such as a hot toddy.

Quite a number of drugs have more or less reputation as diaphoretics. The acetates of potassium and ammonium, Dover's powder, citrate and bitartrate of potassium, and sweet spirits of nitre have all been advocated for this purpose, but there is no other drug which exerts so noticeable an effect in this direction as jaborandi. Jaborandi may be used as an adjuvant to heat, a dose of the muriate of pilocarpine being n hypodermically at the bath, or it may be given alone and at reg- intervals to keep up a constant mild diaphoresis. In using jabo- di or its alkaloid every precaution to prevent depression must be d, and the physician should be always prepared to resort promptly stimulation in case such an untoward effect occurs. For a child of ree one-fortieth to one-twentieth of a grain of pilocarpine may be ministered every six hours. The effect of the drug is, however, much ore marked when given hypodermically; in this way a child three ears old should receive one-thirtieth of a grain, which may be repeated cording to the necessities of the case.

When uræmia threatens or œdema is increasing at an alarming rate e physician will appreciate the importance of invoking the elimina- ve action of the bowels. Some cathartic must be chosen which will promptly produce copious watery evacuations with as little depression as possible. Calomel is recommended, because it not only acts as a cathartic, but has also a diuretic action. It should be given in one fairly large dose—for a three-year old child, two grains. In the course of three or four hours the calomel should be followed by the administration of sulphate of magnesium. This is best given in saturated solution, small doses being taken at frequent intervals. For a child half a teaspoonful undiluted may be given every half hour until the desired effect is produced. Another preparation which has justly acquired a good reputation is the compound jalap powder. To a child of three, one to five grains can be given, and this dose should be repeated once a day or as often as may be necessary. When the symptoms are very urgent one of the more powerful cathartics may be required, such as podophyllin, elaterium, or croton oil, but these drugs are dangerous and should be used only when milder measures have failed.

The use of remedies to stimulate the action of the kidneys must be limited to those which are non-irritating diuretics. It is frequently of benefit to apply over the region of the kidneys hot poultices. With the poultices are sometimes incorporated drugs for absorption by the skin; thus a poultice of digitalis leaves is recommended. The two drugs which are most appropriate for administration as diuretics are the acetate of potassium and digitalis. The latter causes diuresis by increasing the force of the heart's action, and this often affords an additional indication for its exhibition, as not uncommonly the heart is much weakened by the scarlatinal poison. It has been taught that the infusion of digitalis is a more efficient diuretic than the tincture; the infusion is, however, not a preparation which will keep, and it should be made up each time it is prescribed from perfectly fresh digitalis leaves, so that unless the physician can rely implicitly upon his druggist the tincture will be found the more useful of the two. The acetate of potash and digitalis are usually given together:

℞. Potassii acetatis, ʒij;
Infusi digitalis, ℥iss;
Aquam, ad ℥iij.—M.
Sig. Teaspoonful every three hours for a child three years old.

In the opinion of the writer the drugs which produce diuresis by direct stimulation of the secreting structures of the kidney are not appropriate for the treatment of severe acute inflammation of that organ, such as is the nephritis of scarlatina.

When dropsy of a serous cavity occurs to so great an extent that life is threatened the fluid should be withdrawn by aspiration. It is then often possible to prevent the reaccumulation by keeping up as thoroughly as possible diuresis, catharsis, and diaphoresis. In less severe cases these means alone may suffice to remove the dropsical accumulation, but whenever there is any interference with important vital functions on account of the amount of the fluid, valuable time should not be wasted before employing our most certain means of relief.

Uræmic convulsions demand a thorough and prompt use of all those depurative measures recommended above. In addition we must try to control the convulsions by the exhibition of the bromides and chloral. To a child of three, five grains of bromide of potash may be given every ten minutes until the convulsion ceases, and then at longer intervals to sustain the effect. Chloral is a still more powerful agent. In some cases of convulsions it is impossible to get the patient to swallow. It is then necessary to resort to rectal medication. For a child three years old five grains of chloral dissolved in an ounce of water should be introduced into the rectum with a small syringe, and retained by pressing a cloth firmly over the anus. As an adjuvant the body should be immersed in warm water. When these means fail to control the convulsions, chloroform should be given by inhalation, though in cases of such severity the result will hardly be favorable.

During convalescence from nephritis the patient should be kept in bed clothed in flannel, and not allowed to get up till the urine has been for some days entirely normal. After getting out of bed a careful daily examination of the urine must be made, and upon the reappearance of albumin the patient must be again put to bed. The diet is to be light but nutritious, and suitable to the age of the patient. The administration of an iron tonic is frequently demanded by the anæmia which often follows the nephritis. Basham's mixture is very suitable, and with it small doses of digitalis may be prescribed.

The treatment of some of the sequelæ of scarlet fever has been necessarily considered in speaking of the treatment of the complications. Mention will now be made of the remedial measures which should be used in some of the more important sequelæ to which reference has not been made above. The chronic enlargement of the tonsils which not infrequently follows in the wake of scarlatina should be carefully treated, as this condition constantly exposes the sufferer to all forms of infectious angina. Often the tonsils may be reduced to a normal size by repeated cauterizations with nitrate of silver or the galvano-cautery. If these measures fail, it is best to remove the organs by surgical procedure.

When tubercular infection of the lungs or other organs results from scarlatina, those remedies are indicated which are of avail in tuberculosis under other circumstances. A change to an appropriate climate must be advised, cod-liver oil and creasote prescribed, and surgical interference urged where it is indicated, as in tuberculosis of the bones and lymph ganglia.

r the paralysis of the muscles which sometimes follows scarlatina
nine by the mouth or hypodermically, passive movements, mas-
nd electricity are the methods of treatment at our disposal.
valvular lesions of the heart which result from scarlet fever
re the ordinary treatment of chronic valvular heart disease, a care-
gulation of the life and habits of the patient, and the administra-
of the well known heart tonics when necessary.
Attention has been called to the peculiar anæmia which sometimes
sists without apparent reason after scarlet fever. This condition
nds a nutritious diet and residence in the country, where pure air
plenty of sunshine can be obtained. In addition, one of the
onger ferruginous tonics should be prescribed:

℞. Tincturæ ferri citro-chloridi,	ʒij ;
Glycerini,	ʒiij ;
Aquæ cinnamomi,	℥iij.—M.

Sig. Teaspoonful an hour after meals for a child of three.

It is not possible nor is it necessary to consider the treatment of all the sequelæ which may follow scarlatina. In general it may be said that they demand the same treatment that would be appropriate if they occurred independently, the physician always bearing in mind that the sequel is affecting a person whose vital forces are impaired by the poison of scarlatina.

RUBEOLA—MEASLES.

BY J. P. CROZER GRIFFITH, M. D.

ITION.—An acute, infectious, eruptive fever, beginning with
tarrhal symptoms and later developing a characteristic maculo-
ash.

YMS.—The disease is called *Rougeole* by the French and
y the Germans. The Italian name, *Morbilli*, later became the
ular until recent years, but "rubeola" has now largely sup-
, at least in English. Morbilli is not to be preferred, since it
gnificance as applied to this disease; rubeola is much better, in-
is at least suggestive of the color of the eruption.

OGY.—Measles, if not the most frequent, is one of the most
diseases of childhood. Climate and geographical distribution
ave no influence whatever upon it, and it develops equally
ever the infectious principle has access to the inhabitants. It
ided tendency to prevail in epidemics, which come at intervals
r three years. In large cities, however, cases occur nearly
r, although even in them the epidemic influence is very distinct, and in some years the disease will be far more prevalent than in others. It often happens, too, that its severity in some years is very much greater.

The influence of *age* is not so great as would at first appear. Although principally a disease of childhood, its greater rarity in adults depends solely on the fact that most individuals have suffered from it before reaching adult life. There is no reason to believe that any degree of immunity is conferred by advancing years. Numerous well known and often quoted instances prove the susceptibility of adults to it. Perhaps best known of these is the history of the disease in the Faroe Islands, in which persons of all ages suffered with equal severity. In addition may be mentioned the prevalence of measles among the soldiers in the American Civil War and in the Franco-Prussian War.

On the other hand, infants under six months are comparatively rarely attacked, and this does not seem to be explicable entirely on the ground that they are less exposed to infection. That it may sometimes occur is shown, for instance, by the experience of Embden, who observed 24 cases in children less than six months old in an epidemic at Heidelberg. Thomas collected the reports of 16 cases in which children had been born with the disease, and other instances have since been observed (F. B. Richards, Philpott). Statistics show that the greatest number of cases seem to develop in children from three to eight years old.

Sex cannot be said to possess any special influence, and statistics show no certain differences between the susceptibility of males and females.

Season has a positive power as an etiological factor, the disease being idedly more common in the winter and spring months. This may end upon the greater degree to which children are housed at this and the increased exposure to infection through meeting in ls. The diminished degree of resistance which the state of the n often offers at this time may also have some influence. The astics of Hirsch show that 3390 of the epidemics which he records urred in the cooler weather and only 191 in warm weather.

The only real cause of measles is *infection*. The infectious principle certainly a very active one, for, as stated, nearly all those exposed ontract the disease. Very short exposure is all that is ordinarily reired. The virulence of the infectious principle is so great that if the sease breaks out in a school or other institution for children, it is usually impossible to stop its spread. The poison is certainly very diffusible, and is probably oftenest carried by the surrounding air and deposited upon the respiratory mucous membrane of those about to be attacked. It may be desiccated nasal or bronchial mucus which contains the poison thus transmitted, for inoculation experiments with nasal mucus applied to the mucous membrane of children appear to have been successful (Mayr). Other experiments of a similar nature have indicated that the tears and saliva contain the infectious principle. On the other hand, although it has been commonly supposed that the desquamating skin was decidedly infectious, inoculation experiments do not indicate that this is the case (Guinon). There is an element of doubt about some of the inoculation experiments reported, but the investigations with the blood are quite convincing, since nearly all observers agree that the disease can be produced by inoculating with it.

It is possible for the infection to be carried by the clothing of the sick or by a third person from the sick to the well, and numerous instances have been reported in which this has occurred. This method of transmission is, however, certainly uncommon, and it is very unusual for a physician to carry the disease from house to house. The vitality of the infectious principle is comparatively brief, for infected clothing soon ceases to be dangerous. Home found that clothes saturated with the blood taken from cases of measles lost their infecting power in ten days, although in these the poison was probably present in its most virulent state.

Measles is infectious at all periods of the attack. The power of infection probably exists during incubation, and is certainly very active during the prodromal stage. It persists during the stage of eruption and is least strong in the desquamative stage.

PATHOLOGY.—Analogy to other infectious diseases whose cause has been found to be a pathogenic microbe would certainly indicate that some such organism is present in measles also. Observations have, however, as yet led to no positive conclusions. The earlier investigations have ceased to possess much value in the light of recent bacteriological methods. There is no proof that the various bodies which were discovered in the blood, sputum, or breath by different observers had any real connection with the disease. Among later studies those of Canon and Pielicke are interesting. These observers discovered a bacillus in the blood and nasal mucus of 14 morbillous patients. They succeeded to a limited extent in making cultures of them in bouillon. Subsequent investigations by Laveran and by Josias have not confirmed their results. Doehle reports the presence of a flagellated parasite which infests the red corpuscles and the plasma. Other writers, among whom are Cornil and Babes, have described micro-organisms found in the lungs of patients dead of pneumonia after measles, but it does not appear that these were in any way the cause of the measles itself. So, too, Méry and Boulloche found the pneumococcus and a streptococcus in unusual numbers in the saliva in cases of measles, and believe that this accounts for the tendency to respiratory complications. It is clear that the nature of the cause of measles needs further study.

There are no pathological lesions characteristic of measles. There exists some cellular infiltration of the skin around the vessels of the cutis, the sebaceous, hair, and sudoriparous follicles, in the superficial layer of the papillæ, and in the Malpighian layer. There is a catarrhal inflammation of the larynx with swelling and redness and cellular infiltration, and sometimes ulceration also. The lining of the trachea and bronchi exhibits inflammation of varying intensity. The different types of pneumonia described as attending measles have no anatomical features distinguishing them from broncho-pneumonia produced in other ways. The mucous membrane of the alimentary tract and of the eyes is subject to the swelling and small-celled infiltration of catarrhal inflammation. Sometimes Peyer's patches are much swollen.

SYMPTOMS.—*Stage of Incubation.*—The length of time between the entrance of the germs into the system and the appearance of characteristic symptoms is a period not subject to much variation, although there seem to be occasional exceptions to this. The duration has been determined by direct inoculation experiments performed by Home, Mayr, and others. There have been besides numerous instances in clinical experience in which the duration of incubation could be accurately determined; but the most valuable published reports are those of Panum upon measles in the Faroe Islands. The majority of observations agree in fixing the incubation at ten to twelve days until the first appearance of symptoms; most of the variations from this which have been reported depending upon the difficulties in determining just when infection has occurred.

There are, as a rule, no symptoms to be observed during the period of incubation. Rarely there is slight fever, headache, malaise, or loss of appetite for some days before actual evidences of the disease begin, but in the majority of cases these symptoms cannot with certainty be attributed to the action of the germs upon the system.

Stage of Invasion.—In typical cases the prodromal symptoms last three days, and are quite characteristic, the eruption appearing upon the fourth day. The child is irritable, fretful, feels tired, is indisposed to play, and is often chilly. There is often a very decided and almost characteristic drowsiness. The most important symptoms are the fever and the catarrh of the respiratory apparatus. The conjunctivæ, particularly of the eyelids, are red and swollen, the sclerotics are injected, there are lachrymation and photophobia. There are running from the nose, obstruction to respiration through it, sneezing, and sometimes nosebleed. The voice is hoarse and a hard, dry, and often distressing cough is present. Auscultation shows but a few dry râles, or none at spite the severity of the cough. All the catarrhal symptoms marked by the second day, and they increase in severity ut the prodromal stage.

fever of the stage of invasion is rather irregular. Generally is some elevation of temperature from the first day of the disease, this may be very considerable. Afterward it runs a variable se. Perhaps in most cases it goes steadily upward, with a morning nission, but in others there occurs a very decided remission, or even ermission, of both morning and evening temperature, usually on the ond, third, or fourth day, followed by another rise. This curve has n described by some writers as that characteristic of measles, but it nnot properly be called so.

Among other symptoms of the invasion those of the alimentary tract e important. The tongue is coated, but exhibits nothing characteristic. tonsils are slightly swollen, and the mucous membrane covering em, the pharynx, and the fauces is red. By the second or third day of the prodromal symptoms spots which have been called the "enanthema" appear, especially on the uvula and soft palate, but often extending over the lining of the cheeks, the hard palate, and even the lips and the gums. They have also been found on the mucous membrane of the larynx and on that of the eyes, and have even been seen at autopsies in the small intestine (Steiner). The spots are deep red in color and of the size of a pinhead to that of a split pea. They last several days, or may disappear before the eruption on the skin shows itself. They are, indeed, entirely analogous to the latter, and are really of the same nature.

There are loss of appetite, thirst, often slight sore throat, and sometimes vomiting. The bowels may be either constipated or loose. Sometimes there is irritability of the bladder with frequent desire to pass urine. Occasionally there is delirium in this stage, and, rarely, convulsions. Enlargement of the lymphatic glands in different parts of the body is a not infrequent symptom. In an earlier publication[1] the writer called attention to the fact that examination would almost always show an enlargement of the superficial cervical glands in cases of measles, and that this enlargement could not therefore be relied upon as a diagnostic symptom of rubella.

Stage of Eruption.—The rash generally first becomes visible during the night, and is found when the child wakes upon the morning of the fourth day. Close observation will show, some hours before the macules actually develop, a not easily described alteration in the appearance of the skin of the face—an indistinct redness, or as though there were an indefinite roughness or mottling situated beneath the surface. I have frequently had nurses call my attention to this, and predict, with correctness, that the typical rash would be present by the next day. The rash first appears upon the forehead, cheeks, temples, about the ears and the mouth. Just what part of the face is first attacked is variously stated. It probably differs in different cases. The eruption consists of pale red macules, at first not perceptibly elevated, round, oval, or irregular in shape, and of pinhead to pea size and separated from each other by healthy skin. The number of these rapidly increases, and their color generally grows more intense until they become deep red, often slightly tinged with purple. They also become distinctly elevated to the finger if not to the eye, although careful examination usually shows that the elevation is visible as well. Not infrequently, especially in very mild cases, the eruption preserves its pale red color. By the second day of its appearance it has spread over the whole body, perhaps with the exception of the legs and forearms, which may not show it until the third day, and it is yet more abundant in the situations where first seen. In certain regions, especially on the face, inner surfaces of the thighs, and the back, or wherever there is much hyperæmia, the spots become confluent in large areas. Still, however, the appearance is characteristic, for the skin is somewhat infiltrated and unequally rough, and the color is not evenly intense, as it would be in scarlatina. Besides this tendency to confluence there is seen all over the body a peculiar and very characteristic disposition of the individual papules to group themselves into irregular, short, straight, or oftener curved lines, constituting the well known "crescentic" eruption of measles.

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[1] *Univ. Med. Magazine*, June, 1893.

The individual spots reach their fullest development in about twenty-four hours and then begin to fade. When first seen pressure with the finger causes them to lose their color momentarily, but later this is not the case and a faint yellowish tinge remains. The eruption as a whole is most intense on the second or third day. Then it begins to grow paler, beginning in the regions where it first appeared, and assumes a somewhat brownish and finally a yellowish color. All trace of the spots generally has disappeared in four to five days from their first development.

By the second day of the eruption the face presents a decided puffiness, which, with the inflammation of the eyes, gives a heavy and stupid expression that is very characteristic of the disease. The temperature still ascends as the eruption develops, or, if it has previously fallen, goes up again and continues to increase for the first two days, with the morning elevation slightly lower than the evening one. It attains its height when the eruption is at its maximum. On about the third day of the rash it begins to fall rapidly to normal, although sometimes the descent is more gradual and the normal is not attained for four or five days after the fall begins. Crisis is, however, the rule. The persistence of the catarrhal symptoms probably has much to do with the existence of the fall by lysis.

The pulse is increased in proportion to the temperature, and the respiration likewise, unless influenced by respiratory complications.

The catarrhal symptoms of the initial stage persist or even increase in severity during the first part of the stage of eruption. Coryza and photophobia are often very severe; the cough may be distressing and often croupy, and the voice hoarse and even whispered. As the disease advances examination of the chest reveals numerous mucous râles of different sorts. The discharge from the nose is thin and acrid and irritates the lip over which it runs; later it becomes purulent. Nose-bleed is not uncommon. The secretion of the bronchi is tenacious, and only grows purulent as the severity of the attack decreases. In most cases there is no expectoration, owing to the early age of the patient.

Most of the catarrhal symptoms grow less with the fading of the tion, but the cough and hoarseness often tend to persist a little er.

The tongue is moist and coated with a white fur in nearly all in- ces. In some severe cases, however, although uncomplicated, it may ry or even denuded of epithelium, as in scarlet fever. The throat ten sore, and the pharynx, tonsils, and palate are hyperæmic. Ap- ite is diminished or gone, but thirst is greatly increased and is often st intense. Vomiting sometimes occurs, but is not frequent. On other hand, diarrhœa is a very common symptom ; it may develop any time during the eruptive stage and may be severe.

The urine is reduced in amount, is high colored, and is voided quently. It occasionally contains albumin during the height of e fever. Acetonuria has been reported by several observers, and ropeptonuria by Loeb. [illegible] tion is particularly well marked in measles. I have found it [illegible] every case examined.

Enlargement of the ly[illegible]ands of the body is of common occurrence, especially of those [illegible] neck.

A tendency to drowsiness often persists during the height of the disease. Slight delirium, especially at night, is very common.

Stage of Desquamation.—This may be said to begin with the disappearance of the eruption, although the scaling itself may not take place until a day or two later—on the average the tenth or eleventh day of the disease. The desquamation consists of very small branny scales or dust, entirely different from the peeling or stripping which occurs in scarlatina. In severe cases it may be quite extensive, but as a rule it is most marked on the face and is slight, and very often cannot be detected at all or only if carefully looked for. It lasts but a few days.

ANOMALOUS FORMS.—Measles is subject to a great number of variations either in certain particulars or in the course of the disease as a whole. Some children are scarcely sick at all, but the majority are not fit to be out of bed. Occasionally the duration of incubation seems to vary from the normal, and may be either longer or shorter than the figures given. The stage of invasion may be much prolonged (sixteen days, Barthez), but it is oftener either abnormally short or marked by so few symptoms that it is overlooked. I have seen house epidemics in which the invasion was so little marked in all the cases that the diagnosis of the disease was at first rendered obscure. In the fully developed disease we may have several different varieties. The mild form exhibits a very short course with well developed or poorly developed eruption and very mild symptoms. The patient is not confined to bed and may have scarcely appreciable fever (*rubeola afebrilis*). In the abortive form the stage of invasion may have been well developed and all its symptoms pronounced, as were those of the eruption stage at the outset, but the eruption and its attending symptoms disappear with remarkable rapidity. A variety without eruption, *rubeola sine eruptione*, has often been described. This can be recognized only when it occurs in school or house epidemics, exhibits all the symptoms of the disease except the rash, and confers a future immunity against it. Similarly, a *rubeola sine catarrho* has been described, in which the eruption is present, but without catarrhal symptoms either attending it or preceding it during the period of invasion. There is not much doubt that the great majority of such described cases were in fact instances of rubella or of some affection of the skin not of the nature of measles. It could only be in house epidemics where it was certain that rubella was absent, or in cases in which rubella had previously occurred, that the diagnosis could be made. On the other hand, with the capability which measles has to vary there is not much question but that this form is sometimes seen.

Grave or malignant forms of measles may show themselves in various ways. One of the best known is hemorrhagic measles, or "black measles" as it has often been called by earlier writers. It is now a rare disease. It occurs only in debilitated subjects living under imperfect hygienic conditions, as in prisons, camps, asylums, and the like. The eruption never develops well and soon becomes pale. Hemorrhages of different size now take place into the spots and elsewhere under the skin, as well as from the urethra, vagina, nose, intestine, and other mucous membranes, and even into the muscles and from serous membranes. There is profound adynamia, delirium, and stupor. The disease is very fatal and its course very rapid, although recovery may occur. In another severe variety, which may be called the ataxic or typhoid form, the poison appears to have produced great depression of the system. There are high fever, rapid, weak pulse, feeble circulation, dry tongue, rapid breathing, great prostration, restlessness with subsultus, low delirium and often convulsions, and finally coma. In this form, as in the last, the rash is poorly developed, or, if well out at the first, rapidly disappears with the onset of the grave symptoms.

Rubeola occurring during the course of other affections may run a very abnormal course. The invasion may be unnoticed, the eruption poorly developed, and the symptoms severe. So, too, when some intercurrent disease appears during an attack of measles the rash may rapidly recede.

There are numerous minor variations seen in measles depending upon characteristics of the eruption. Sometimes a rash appears, especially about the head, almost at the beginning of the invasion, and resembles that of measles except that it is pale. It may remain unchanged or perhaps grow paler still, and then be replaced at the proper time by the regular eruption. Such cases are apt to lead the physician to believe at first that the case is one of rubella or that he has to do with a mild instance of measles. Sometimes the rash develops upon the face after appearing first upon the trunk, or it may become visible only on certain parts of the body. The recession of the rash has already been referred to. It may take place early in the attack in some severe or complicated cases. The reappearance of the rash is then a favorable sign. An ecchymotic eruption is of common occurrence. It is seen in those cases in which the rash has been very well developed. It is due to extravasation of blood into the spots or to the decomposition of red blood corpuscles which have exuded from the vessels. The deep bluish purple spots thus produced, which do not disappear on pressure, and which occur in greatest numbers on the extremities, remain long after the patient has recovered in all other respects. Traces of them may be seen for as much as a week or two. This form of eruption has nothing

mon with hemorrhagic or purpuric measles, and is not
y especially severe symptoms.

PLICATI ONS AND SEQUELÆ.—The most important complica-
re those connected with the respiratory apparatus. Spasmodic
sometimes occurs. Ulceration of the larynx, possibly with
of the glottis, is an unusual complication. Diphtheritic laryn-
sometimes develops. Chronic coryza may remain as a sequel.
e exhausting epistaxis may occur. Bronchitis in moderate degree
ymptom of the affection, but not seldom it becomes so severe that it
rves consideration more than the measles does, and is then to be
ded as a serious complication. Still oftener it is a sequel, and con-
s after other symptoms have disappeared, being the cause of the
stence of more or less fever for a considerable time. In infants it
prove fatal, principally by inducing atelectasis.

roncho-pneumonia is a frequent and very dangerous complication
infancy and early childhood. It may develop at any time during the
tack, but oftenest as the eruption is fading, or as a sequel after a week
two, and only infrequently during the invasion. It is recognized by
e failure of the fever to disappear at the proper time or its reappearance if the temperature has already fallen, and by the increase in the severity of the cough, the rapidity of the respiration, and the development of other characteristic symptoms of pneumonia in children. Often the condition is really a tubercular broncho-pneumonia. Croupous pneumonia is also a complication or sequel of measles, but is of much less unfavorable prognosis and is less common than the catarrhal form. Pleurisy is of rare occurrence. Phthisis pulmonum is a very frequent sequel.

Complications situated in the intestinal tract are often present. The drying and peeling of the tongue seen in severe cases have already been mentioned. Catarrhal, aphthous, and ulcerous stomatitis may occur, the latter oftenest as a sequel, especially in debilitated and cachectic subjects. Noma is an occasional sequel oftener produced by measles than by any other disease. The occurrence of measles predisposes to the development of faucial diphtheria, which is not uncommon as a complication or sequel. Occasional vomiting and frequent diarrhœa have already been referred to as symptoms of measles. The diarrhœa may become a serious complication depending on entero-colitis; this occurs especially in debilitated subjects or during the heat of summer. Sometimes the disease is dysenteric or choleriform; not rarely a chronic diarrhœa persists as a sequel.

Endocarditis and pericarditis are rare. A suppurative pericarditis has been reported by several observers.

Nervous affections are unusual. The occurrence of convulsions, delirium, and the like has already been noted. Convulsions during the course of the attack are often an indication of the onset of some complication. Tubercular meningitis is a sequel. Paralyses of various forms may follow measles. Allyn has collected over 40 cases of this nature. Maniacal seizures, tetanus, and strabismus have been reported in rare instances.

Chronic conjunctivitis, iritis, blepharitis, keratitis, and other affections of the eye are prone to develop, especially as sequels. Catarrhal or purulent otitis media not rarely accompanies or follows measles, although less often than it does scarlatina. Disease of the labyrinth has been reported.

The occurrence of albuminuria as a symptom has been mentioned. A true acute nephritis following the attack has been observed, but is certainly very exceptional. Ulcerous vulvitis is an uncommon, and noma pudendi is a rare sequel, but measles distinctly predisposes to their development. Very rarely gangrene has been observed on other parts of the body. Other affections of the skin sometimes complicate or follow the disease. Miliaria and sudamina sometimes appear when the eruption is at its height. Impetigo or abscesses are occasional sequels. Herpes zoster has been seen with measles. Vesicles or bullæ sometimes accompany the rash. Subcutaneous emphysema has rarely been reported. Tuberculosis of the bronchial or mesenteric glands may be a sequel. Dropsy, necrosis, progressive emaciation, and other and various conditions have occasionally been reported.

Measles may complicate or be complicated by any other acute or chronic disease. The influence which other diseases sometimes have upon its course has been referred to in discussing the variations in the symptoms. On the other hand, measles occurring in the course of pneumonia, bronchitis, or tuberculosis aggravates greatly the severity of the previous affection. It seems to render some disorders less severe or even to cause them to disappear. Thus Barthez and Rilliet have seen chorea, incontinence of urine, and epilepsy cease after the occurrence of measles. Eczema and some other skin affections may disappear when measles is present, and, although liable to come back when the disease is over, they may stay away permanently.

Measles may be combined with various infectious diseases, and cases have been reported in which it has occurred with variola, varicella, vaccinia, scarlatina, typhoid fever, rubella, and mumps. As above stated, it not infrequently is complicated by diphtheria. The frequency of the combination of whooping cough and measles or the following of one by the other has long been well known. The association renders the prognosis of either decidedly worse. Just what the etiological relation is, or whether there is indeed any, is not certain.

RELAPSE AND RECURRENCE.—Rarely a relapse may occur. This takes place either during the attack or during convalescence, in the course of the second, or possibly even the fourth, week. Sometimes all the original symptoms are reproduced in a characteristic state. In other instances the second eruption may be very pale, and last not more than twenty-four hours, while the catarrhal symptoms and fever are absent or very slight. Relapses are certainly much rarer than reported cases would seem to indicate. A large number of the supposed instances are probably errors in diagnosis, but this does not apply to all of them.

One attack of measles almost certainly protects from subsequent ones. There is not much doubt that most of the children who are stated to have had two attacks of measles suffered from some other affection upon one of the occasions. At the same time two distinct and genuine attacks may sometimes occur, and instances of this have been reported by well known and careful observers. Duchesne has recently a an instance of three well marked attacks occurring within two

IAGNOSIS.—The diagnosis of measles, taken as a whole, rests upon long prodromal stage with its attending fever and catarrh, and upon esence later of a characteristic eruption. In the initial stage it is sible at first to do more than suspect the development of measles. egree of fever which accompanies the catarrhal symptoms seems n to be too great for an ordinary cold. It is, however, what might xpected in a case of influenza, and from this disease the initial stage easles can sometimes hardly be distinguished. So, too, a severe chitis will produce high fever, but is more apt in young children to attended by numerous râles in the chest. The discovery of the nthema on the mucous membrane of the throat and mouth renders diagnosis certain. When the eruption appears the diagnosis is enerally easy, and yet even now difficulties sometimes arise in cases hich are not quite typical.

Rubella is the disease which most resembles rubeola. It is to be distinguished by the shorter and much less severe initial stage, the paler, more fugacious, and more multiform character of the eruption, which does not tend to arrange itself in crescentic forms, and the less intensity of the symptoms attending the eruptive stage. (See table of diagnostic symptoms in article on Rubella.) In sporadic cases, however, the diagnosis between the two diseases often cannot be made.

Scarlatina can never be confounded with measles in typical cases. In the initial stage of the latter affection the sore throat, if present with the fever, might suggest scarlet fever. There is not the rapid onset with unusually rapid pulse, the absence of catarrhal symptoms, and the great tendency to vomiting which characterize scarlet fever. In anomalous cases of scarlet fever the eruption is sometimes patchy and resembles measles decidedly; while, on the other hand, measles may become very confluent and may at first sight look like scarlet fever. Such confusion is more theoretical than real, for the character of the other symptoms will rarely leave any difficulty in diagnosis. In the stage of desquamation the differences are very distinct, for the scales of scarlatina are in flakes, while those of measles are dustlike or branny.

Typhus fever has an eruption which is strikingly like that of measles, especially when the rash of the latter becomes ecchymotic. There is, however, an absence of coryza and of conjunctivitis, while the presence of mental torpor, the slight development of the rash on the face, and the persistence of fever for so long a time help to distinguish typhus fever.

Typhoid fever sometimes has such numbers of spots that it bears a superficial resemblance to a poorly developed eruption of measles. The diseases are distinct in every other particular.

Variola can only resemble that form of measles in which the eruption is unusually papular, isolated, and hard, and then the resemblance is of brief duration only. It is close enough, however, to have caused serious blunders. The rash is harder and more shotlike than that of measles ever is, the papules become vesicles by the third day or earlier, and the temperature curve is characteristic. In the period of invasion, too, smallpox exhibits intense headache, pain in the back, vomiting, and an absence of catarrhal symptoms.

Varicella is distinguished by the rapid development of vesicles, as well as by the absence of catarrhal symptoms.

There are various eruptions, not symptoms of the infectious fevers, which may resemble that of measles. Prominent among these are some of the medicamentous rashes, notably those sometimes produced by antipyrine, copaiba, quinine, chloral, etc. As a rule, the fever and the catarrhal symptoms are absent, but sometimes, especially in the copaiba and antipyrine eruptions, both may be present and the similarity to measles may be striking. The eruption is not, however, purely that of measles, but is more or less multiform. There is the absence, too, of an initial stage. In infants the presence of catarrh, combined with some of the erythematous rashes to which children of this age are liable, may simulate mild measles closely. In adults forms of erythema may resemble measles, but usually not closely, and the multiform nature with the absence of characteristic initial and attendant symptoms serves to distinguish them.

PROGNOSIS.—The prognosis of measles is usually excellent, but varies with the epidemic and with the individual, and is especially influenced by the presence or absence of complications. An average mortality would be 3 per cent., but there have been series of cases with a mortality of over 30 per cent. (36.7 per cent. in the siege of Paris; Colin). The younger the patient the graver the prognosis. This applies particularly to children, for adults are often very severely attacked. This has been exemplified, for instance, in the American Civil War, the Brazilio-Paraguayan War, the Franco-Prussian War, and among savage nations. In such cases, however, we have another important element influencing the prognosis—namely, the effect of exposure, want, crowding, and other elements of imperfect hygiene, combined with lack of nursing and often with the existence of previously debilitated health. Such conditions, too, account for the high rate of mortality often seen in foundling asylums and in homes, hospitals, and other institutions for children. It is not only that the hygiene is not always perfect, but that the previous debilitated condition of children of this class, which existed before they entered the institutions, has rendered them less able to resist the effect of the disease.

The combination with measles of any other previously existing disease, such as scarlatina, tuberculosis, bronchitis, whooping cough, dyspepsia, rachitis, atrophy, etc., renders the prognosis much more unfavorable. In fact, the development of any complication adds greatly to the gravity of the affection, for it is to the complications that the mortality is almost entirely due. Broncho-pneumonia is probably the complication which kills the most children, but atelectasis, croupous pneumonia, and diarrhœa carry off a great many cases.

Unfortunately, even after the patient has apparently recovered entirely the danger is not over, for the sequels of the disease, notably tuberculosis in some of its forms, weaken the constitution and may at last prove fatal.

TREATMENT.—*Prophylaxis.*—The fact that measles is contagious before any symptoms appear renders prophylaxis almost impossible. Once the disease has broken out in a family or institution, it is seldom that its spread can be controlled. Nevertheless, the effort should always

An affected child should be isolated immediately after the
spicious symptom has been noticed. The room should be at the
the hou away from other susceptible inmates of the household,
ded furn re and hangings are better taken away. All soiled bed
dy linen hould be disinfected. There should be as little com-
tion as possible with other parts of the house, and the attendants
the sick would do well to confine themselves to the room, only
g it when going out of the house for rest and recreation. In fine,
dinary means of disinfection and isolation used in nursing infec-
diseases should be followed, although there is not as great danger
rrying the disease as exists in the case of scarlatina and some other
ders. Although it is not certain that the scales of the desquama-
possess any infectious power, it is best to give the patient a hot
nfecting bath after about the twelfth day of the disease. Quaran-
should last for at least two weeks from the onset, and three weeks
much safer period. After the room is vacated ordinary airing and
aning are all that is needed, since the measles germ is short lived.
l more careful disinfection, as by burning sulphur and washing the
walls with disinfectant solutions, can be used if desired, and after
malignant cases it is best to do this. Other children of the family
should not go to school until after fourteen days from the time the
sick child was isolated—not so much to avoid the carrying of the germs
in their clothing, since this is not likely to occur, as because they may
hemselves be going through the incubative process and be soon able to
ransmit the disease to others. If one can be sure that the disease has
already been contracted, it is well to remove children entirely from
locality where measles is prevailing. This is especially true if they
are debilitated from any cause.

Treatment of the Attack.—In mild cases very little treatment is required, and in any event it must be purely symptomatic. As soon as symptoms appear the patient should be confined to one room, as stated, and, better still, to bed. The temperature of the room should be equable, at 68° to 70° F., and there should be no draughts. At the same time it is absolutely necessary that there should be abundance of fresh air, previously warmed if possible. The child should be covered only as warmly as is comfortable to it. Far too often the bed is heaped with too much clothing. About the close of the third day a warm bath may be given, as it tends to relieve the fever, to quiet the nervous system, and to aid a satisfactory development of the rash. At all times water must be used in a manner to ensure cleanliness. There is no need of shunning water in the way that is sometimes done. Ablution, if performed properly, never need do harm. The same remark applies to the changing of the bedclothes and the garments of the child, which popular prejudice causes to be too much neglected.

Liquid or semi-liquid diet is to be recommended, but it is not necessary in the case of older children with undisturbed digestion to use an absolute milk diet. In cases of gastric irritability predigested or other special food may be needed. Water may be given freely in any reasonable quantity to assuage the severe thirst. Infants must be given water without fail, to prevent their overloading their stomachs with milk. Cool, slightly acid drinks may be given to older patients, or alkaline or carbonated waters; or, in case the skin is dry and the kidneys not acting freely, hot drinks. In order to relieve the photophobia it is necessary to keep the room darkened or the patient's eyes turned away from the light and shielded by a screen.

With regard to medicinal treatment, very little is required in ordinary cases. The cough is often distressing and demands sedative mixtures. Small, frequently repeated doses of a combination of opium and ipecacuanha, with sweet spirits of nitre or citrate of potash on account of the fever, answer the purpose very well. As the disease advances and the cough grows looser expectorants may be substituted. Some bromide salt, combined with other drugs, is also an excellent remedy for cough. Fever ordinarily needs no special treatment, even when it reaches as high as 104° F., provided this elevation occurs at the height of the eruption, is not continuous, and is unattended by threatening symptoms. The effect of the fever rather than its degree constitutes the indication for treatment. In ordinary cases the use of nitre or citrate of potash, as mentioned above, is sufficient. When, however, this does not succeed, and the fever is accompanied by tossing, delirium, gritting of the teeth, twitching of the muscles, or, on the other hand, by stupor and unconsciousness, more active measures are needed. A warm bath is often very efficacious. Still more powerful is the action of the cold bath and of antipyretic drugs. The cold bath constitutes a rigorous treatment for children, yet the experience of Fodor, Dieulafoy, and others shows that it is often well borne and very effectual in malignant cases with hyperpyrexia.

We are, however, fortunate in possessing in drugs of the antipyretic class a very valuable means in ordinary cases of attaining the end desired in a less disagreeable way. It is, after all, upon the threatening nervous symptoms that we wish to act in most cases. I have elsewhere published[1] some cases illustrative of the powerful and favorable action which drugs of this class exert upon nervous symptoms. Delirium may be stopped and impending convulsions aborted by small doses of antipyrine, phenacetin, benzanilid, and similar remedies, sufficient in amount to produce slight reduction of temperature, but not sufficient to cause any excessive fall with coldness of skin or profuse perspiration. Such an effect is not needed and is not desirable. Nervous symptoms may also be favorably influenced by the bromides in full doses.

It is important to attend to the condition of the bowels. Constipation is sometimes present and must be relieved. This must be done carefully in view of the tendency patients with measles have to the development of diarrhœa. Enemata are to be preferred, and, if they are not sufficient, mild laxatives, such as castor oil, calomel in small dose, or rhubarb, may be given. Should there be slight diarrhœa, medication is hardly needed. If more severe diarrhœa exists, bismuth with or without opium may be required.

Vomiting does not often call for treatment. Allowing the stomach to rest for a time is often the best of measures, and after this attending carefully to the character of the food. If this does not avail, some of the various remedies commonly used to control it may be employed.

The irritation of the eyes is best treated by diminishing the amount ight in the room. A boric-acid eye lotion used frequently is often lief. The application of a little vaseline to the edges of the lids will vent their adhering during sleep. The spraying of the nose with k tepid alkaline solutions is grateful.

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[1] *Transac. Amer. Pædiat. Soc.*, vol. v.

Failure of the strength in bad cases of measles is to be combated by se of stimulants, sinapisms, hot mustard foot baths and general hot stard baths, with digitalis, quinine, and other tonic remedies. The ession of the rash may be treated by warm baths, although it is to borne in mind that this symptom probably indicates the development some complication which most be sought for and appropriately ted. In general, complications must receive the treatment proper them, and cannot be considered here.

As the patient is convalescing the diet can be increased, but confinement to bed, except in very mild cases, should continue for at least ten days from the onset of the disease, and the confinement to the room for two weeks. This is with reference solely to the patient and without regard to the question of quarantine. The first outing should be made in good weather, and the patient must be well clothed, for the mucous membranes are left in a sensitive state after the attack. Tonic treatment, including cod-liver oil, is often needed during convalescence, and a change of air is very desirable if the full degree of health does not promptly return.

RUBELLA.

By J. P. CROZER GRIFFITH, M. D.

SYNONYMS.—The disease has been known by many names, of which "rubella" seems to be the only one free from objection. The term "rubeola" is applied to it by German writers, but, as it is commonly used to designate measles by English physicians, it is better to restrict it to the latter disease. Rötheln is also a German name for it, unsuitable because it is a foreign word and one especially difficult of pronunciation for the English tongue. "Roseola" is a generic term carelessly applied to rashes of many kinds, and even with the prefix "epidemic" it is not entirely free from objections. "Rubella," has the double advantage that it causes no confusion, since it has been employed in no doubtful sense, and that it is a diminutive of "rubeola," and thus indicates the relationship of the disease to measles (rubeola) a relationship akin to that of varicella and variola.

DEFINITION.—An infectious febrible disease exhibiting a characteristic maculo-papular rash, sore throat, and mild catarrhal symptoms, and running a definite limited course.

ETIOLOGY.—*Age* is an important predisposing cause. The great majority of cases occur during childhood, especially between the ages of five and fifteen years. The disease very rarely attacks infants, yet instances do occur, and a case is reported in which it developed a few days after birth, and in which it would seem that the infectious principle had been transmitted from the mother to the fœtus (Scholl). Adults are not infrequently attacked, yet certainly seem to possess a less marked disposition to contract it. A case in a woman of seventy-three years was observed by Seitz.

Sex appears to be without etiological influence.

The affection occurs especially in epidemics, which are oftenest seen in winter or spring. It is not yet certain whether the malady is a cyclic one, as Thomas thought probable, coming in epidemics at intervals of some years, but it would seem that this is very likely the case. Infection is the only directly exciting cause. The degree of infectiousness has been a matter of dispute, some observers believing it to be but slight, while others claim that the disease is even more infectious than measles. My own experience is entirely in accord with those who hold that its infectiousness is great. The infectious principle is probably transmitted by the breath and by exhalations from the skin, but it seems probable that it can also be carried by infected clothing. The stage at which the disease is most infectious is not definitely known, and opinions differ regarding it. It is certainly infectious very early in the attack, even during incubation, and probably continues so during desquamation and longer.

PATHOLOGY.—The exact position of rubella among the infectious ses was long a matter of dispute, and some writers have even ied that it did not belong at all to this class of disorders. At it was looked upon as a form either of measles or of scarlatina or hybrid of the two, but gradually its existence as an independent tious disorder has been recognized, until at the present time the at majority of observers have no doubt about the matter. Statistics questionably show that rubella is an infectious fever and not a mere ption of the skin; that it appears in epidemics which hold no ation whatever to epidemics of measles or of scarlatina; that it tacks indiscriminately and with equal severity those who have suffered om either or both of these two affections, and that its previous occur- ence does not prevent either of them from developing; that it occurs ut once in an individual, and never communicates anything but rubella to others; and, finally, that its symptoms and course differ from those of ther scarlatina or measles. These points are quite sufficient to establish as an independent infectious disease. Analogy suggests that some microbe is the causal agent in producing it, but the earlier observations which recorded the presence of a micrococcus in the blood were not attended by culture and inoculation experiments, and have not been confirmed by later investigations. The real nature of the infectious principle is therefore still unknown. Post-mortem examinations are only to be had on cases dying of complications, and reveal nothing bearing upon the disease itself.

SYMPTOMS.—*Incubation.*—The stage of incubation appears to vary considerably. This variability constitutes one of the characteristics of the disease as contrasted with the more fixed period of measles. In cases in which I have been able to determine accurately the period of incubation it has varied from five to eleven days. As an average estimate based upon the experience of many observers it may be stated to extend from one to three weeks. There are usually no symptoms complained of during this time. I have occasionally observed very decided enlargement of the superficial cervical glands. Squire states that some complaint of the throat is occasionally made and that epistaxis and enlargement of the post-cervical glands may be noted.

Invasion.—The symptoms of this stage are generally either absent or so slight that they are overlooked entirely. When present they consist of slight malaise, slight cough, suffusion of the eyes and coryza, frequently some sore throat, very commonly enlargement of the superficial cervical glands, occasionally nausea, hoarseness, pains in the limbs, drowsiness, and œdema of the face, and an elevation of temperature of 1° or 2° F. These prodromes last but a few hours, or at the longest not more than a day. I have but once seen them last as long as forty-eight hours. A number of observers, however, have observed them continue three or even four days, and sometimes be severe, but such cases cannot be looked upon as other than anomalous.

Rarely unusual prodromal symptoms show themselves. Among those reported are vomiting, convulsions, delirium, hemorrhages from the eyes and ears, epistaxis, dizziness, fainting, crouplike attacks, intense headache, rigors, urticaria, erythema, or some unclassified prodromal rash.

Eruption.—Very often the child on waking in the morning is found to be extensively covered by the characteristic rash. When, however, the progress of the eruption can be watched from its incipiency, it will generally be found to develop first on the face, and to spread with great rapidity downward over the rest of the body, covering it in a few hours or a day. This is the opinion of the great majority of writers, although a few would locate its first appearance on the breast and arms or the trunk. In a typical case the eruption consists of small, irregularly shaped spots of from pinhead to split pea size, very slightly elevated and of a pale rose tint. The spots are not grouped as in measles. They are widely distributed, closely placed, discrete for the most part, but showing a tendency to become confluent in large areas in certain regions, particularly the face, nates, and flexor surfaces of the thighs. On the trunk the spots are paler, or are brownish red, very small and thickly placed. This is the appearance of the eruption as seen in a typical case. One of the greatest characteristics of the rash, however, is its tendency to vary in different epidemics and in different cases in the same epidemic. This accounts, to a large extent, for much of the confusion regarding the disease, and for the differences in the descriptions which have been given. Some observers report the rash as macular only, and others as slightly elevated. Some describe it as purpler and darker than measles, while most recognize it as paler. Vesicles have occasionally been seen; petechiæ and a purpuric eruption have been rarely reported; a marbled appearance of the skin is mentioned; and a sensation as of shot beneath the skin, which I have observed in one case, was also found once by Clausen. There, are however, two very marked types of variations of the eruption to which I have endeavored, in a former article,[1] to call especial attention under the names of *rubella scarlatiniforme* and *rubella morbilliforme*. In the first the spots are for the most part nearly or fully as large as those of measles, have the same dark red color, and are slightly elevated and more or less grouped. Cases of this sort cannot be distinguished from measles. In the second type the rash is confluent in large patches or almost universally and is not elevated, and resembles scarlatina very closely. Sometimes careful examination in these cases shows a few slightly elevated papulo-macules in the general redness; these are most apt to be noticed on the brows, wrists, and fingers. Even the most careful examination may fail at first satisfactorily to distinguish these cases from scarlatina. All gradations may be found from the normal eruption toward either of these two types. The more papular the rash the greater is the tendency to the grouping of measles, and the more distinctly macular the greater the disposition to confluence. Filatow has gone so far as to describe a rubeoloid and a scarlatinoid form, which he claims are entirely distinct affections. There seems, however, not the slightest doubt that they are really the same disease, as they are produced by the same infection. Many observers have called attention to the likeness of cases of rubella sometimes to measles and sometimes to scarlet fever. In many instances the rash has been scarlatiniform on one part of the body and rubeoloid on another. Ladell reports three such cases, two of which developed scarlatina six months later, and the other measles, thus negativing any possible theory that a nbination of the two diseases had existed. It is, too, of very frequent occurrence for the rash to be papular upon the first day, but to be tinctly confluent, not elevated, and like scarlatina upon the second y.

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[1] *Medical Record*, July 2 and 9, 1887.

The duration of the eruption upon any one part of the body is subct to some variation. In many cases it is often at its height on the ce, neck, and trunk before it appears at all on the extremities, and then s nearly disappeared from these regions in twelve to twenty-four ours by the time it is at its height on the arms and legs. The duration f the full blown rash on any one part is thus from a few hours to half a day. In these cases the rash spreads over the body like a wave, fading from one place while it appears in another. This method of spreading has been considered diagnostic by a number of clinicians, but in certainly just as many cases the persistence of the rash is greater. In such cases it will be found after twenty-four hours still fully developed on the face, while it has extended to the rest of the body; so that the acme of the rash may be said to have been attained everywhere by the second day. The fading then takes place from all parts at once or from the face first, or first from those parts which had been least affected. The total duration of the rash is, of course, subject to considerable variation, depending upon the intensity of its development. The average may be said to be three or four days, although it often lasts a very much shorter time, and may be visible even longer.

The Eruptive Stage.—With the appearance of the rash develop the attendant symptoms of the disease if they have not been present before. They consist chiefly of a combination of slight sore throat with a mild catarrhal condition of the eyes and of the respiratory apparatus. The disagreement between writers regarding the intensity of the symptoms indicates beyond doubt the difference which exists between various epidemics of the disease. Certainly as a rule the catarrhal symptoms are either absent entirely or are very mild as compared with measles, consisting only of slight suffusion of the eyes with coryza and a loose bronchial cough.

Sore throat is a very characteristic symptom nearly always present, yet also nearly always slight. Frequently it is not complained of at all, and is only detected on examination. Oftenest there is only a reddening of the pharynx, and particularly of the anterior pillars, but sometimes the tonsils are much swollen and deglutition is difficult. In not a large number of cases an eruption of punctate brownish red or yellowish red spots are visible over the uvula, soft palate, and lining of the cheeks. Hoarseness is sometimes observed, but is not a common symptom.

The anginose and catarrhal symptoms may disappear entirely after twenty-four hours, and while the rash is still well out, but as a rule they diminish with the eruption. Not seldom, however, the cough and the congestion of the throat persists for some time longer, and an increase of the catarrhal symptoms at the time of the fading of the rash has been reported by Squire.

The temperature of the disease is variable. As a rule, fever is absent or slight, but in some cases, and particularly in some epidemics, it may reach 103° F., or even more. It is at its height on the first or second day of the eruption and diminishes as the rash fades, but sometimes it falls abruptly to the normal on the second day, while the rash is still bright. Indeed, the temperature may fall suddenly or slowly at any time during the attack. Generally the severity of the fever and of the catarrhal symptoms is in proportion to the intensity of the eruption, yet this is by no means an infallible rule. There may be a widespread eruption with an entire absence of fever or with slight catarrhal symptoms, and the converse of this may be equally true. So, too, the acme of the rash and the fullest development of the fever or catarrh are not necessarily coincident.

The rate of the pulse and of the respiration is increased in proportion to the degree of fever.

The tongue is clean or covered with a thin yellowish coating. This is the condition as recognized almost with unanimity by writers. It may be considered a diagnostic point that the tongue never assumes the peeled or strawberry appearance characteristic of scarlet fever. A few writers describe the tongue as similar to that of scarlet fever, but cases presenting this appearance cannot but be considered as altogether anomalous, if, indeed, some of them were actually instances of rubella.

Enlargement of the superficial cervical and posterior auricular glands has long been considered one of the diagnostic evidences of rubella. It is one of the earliest symptoms to appear, being present in some cases even during incubation, and often continuing after the rash has disappeared. I have, however, called attention previously to the fact that this glandular enlargement is not so diagnostic as is often supposed.[1] A similar enlargement, although usually not so great, is very often seen in measles. It is, indeed, very probable that many children, with their natural tendency to this condition, have these glands enlarged independently of the infectious disease. Enlargement of glands elsewhere in the body occasionally occurs.

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Nausea and vomiting are usually considered to be of very rare occurrence. In some of the severest cases they may be present early in the attack, or even be more prolonged, but they cannot be viewed as at all characteristic. The bowels are regular or slightly constipated. The urine, as a rule, contains no sugar or albumin. In exceptional cases there may be a febrile albuminuria, but this is rather anomalous.

Desquamation.—As the eruption fades, spots of a faint brownish or yellowish color often are left and last two or three days. A slight branny desquamation may or may not take place. Some observers have never seen it, and few describe it as more than slight and always furfuraceous. In this respect it is entirely different from the scaling or peeling of scarlatina. The desquamation is generally completed in from one to three days, but occasionally lasts a longer time.

COMPLICATIONS AND SEQUELÆ.—The usual slight import of rubella makes complications and sequelæ uncommon. Those most often seen are affections of the respiratory apparatus. Pneumonia and severe bronbination of the two diseases had existed. It is, too, of very fre- nt occurrence for the rash to be papular upon the first day, but to be inctly confluent, not elevated, and like scarlatina upon the second .

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[1] *University Medical Magazine*, June, 1892.

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Complications and Sequelæ.—The usual slight import of rubella makes complications and sequelæ uncommon. Those most often seen are affections of the respiratory apparatus. Pneumonia and severe bronmay occur. Pleurisy has been reported, as has croup. Most vers have found intestinal catarrh quite unusual. This is in sharp adistinction to measles. It is only in anomalous cases that diar- s seen. Stomatitis has been occasionally witnessed as a compli- as have temporary painful enlargement of the thyroid gland, ia, convulsions, delirium, and rheumatism. Erysipelas, earache, œa, and diphtheria have been described as sequelæ. Among other lications and sequelæ which have been referred to by writers, but are certainly to be considered as purely accidental as they are are varicella, typhoid fever, phlyctenular keratitis, abscesses in rent parts of the body, blepharitis, mumps, tubercular meningitis, nbness and loss of power in the arms and legs, œdema of the legs, iaria, pemphigus, etc.

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[1] *University Medical Magazine*, June, 1892.

RELAPSE AND RECURRENCE.—Relapse is certainly of the greatest ity, and the possibility of its occurrence is not even referred to by e majority of writers. Cuomo saw it in all of the 90 anomalous cases of rubella reported by him, and Kingsley has witnessed it frequently. but with these exceptions the reported cases are rare. It would seem to be most apt to develop from a week to three weeks after the beginning of the first attack. Recurrence is very rare, one attack almost certainly protecting from subsequent ones.

DIAGNOSIS.—The distinguishing of the disease from measles has been discussed more fully under that heading. The most important diagnostic points are the absence or slight importance of the prodromes, their short duration, the absence or slight degree of the catarrhal symptoms of the attack, the slight fever or its irregularity, the presence of more or less sore throat; the greater enlargement of the glands of the neck and behind the ears, and the peculiar characteristics of the eruption. Nevertheless, although the average case can be recognized without difficulty, occasions arise, as has been stated, in sporadic cases where a diagnosis is entirely impossible.

The following table exhibits some of the most important differential symptoms between rubeola, rubella, and scarlatina:

Differential Diagnosis of Rubeola, Rubella, and Scarlatina.

Rubeola.	*Rubella.*	*Scarlatina.*
	INCUBATION.	
Fourteen days.	Very variable; one to three weeks.	One to seven days.
	PRODROMAL SYMPTOMS.	
Usually last three days.	Absent or seldom last longer than twelve to twenty-four hours.	Last twenty-four hours or less.
Severe catarrhal symptoms of nose and eyes; considerable cough.	Catarrhal symptoms, if present, usually slight.	
Slight sore throat not uncommon.	Sore throat often attends.	Marked sore throat.
Vomiting occasionally occurs.	Vomiting very rare.	Vomiting a frequent symptom.
Decided fever, often with a characteristic temperature curve.	Fever absent or slight.	High fever, rapid pulse, marked nervous symptoms.

Rubeola.	*Rubella.*	*Scarlatina.*
	ERUPTION.	
First on the face.	First on the face.	First on the neck and chest.
Spreads gradually; maximum all over body by the second or third day.	Spreads very rapidly; either fading from one part before in full bloom on another, or with universal maximum in twenty-four hours.	Spreads slowly; maximum reached by the fourth day.
Lasts an average of four days.	Lasts three to four days or less.	Lasts six to seven days or longer, sometimes much less.
Color deep red; often purplish.	Color usually pale rose red.	Color intense red; dusky or livid in some cases.
Papular; arranged in irregular or crescentic groupings.	More or less elevated; spots smaller than in measles; discrete or confluent, seldom arranged in groupings.	Minute red points, confluent in large patches or universally.
	SYMPTOMS OF STAGE OF ERUPTION.	
Severe catarrhal symptoms persist and increase; severe bronchitis common.	Slight catarrhal symptoms persist or may appear.	Coryza in bad cases.
Throat sometimes sore.	Slight sore throat nearly always present.	Sore throat a very marked and constant feature.
Superficial cervical and other glands often enlarged.	Superficial cervical and posterior auricular glands nearly always enlarged.	Glands below the jaw often much enlarged.
Tongue coated, in bad cases dry and brown.	Tongue clean or slightly coated; never strawberry or peeled.	Strawberry tongue.
Temperature 102°-104° F.; ascends slowly; maximum with that of eruption.	Temperature variable; seldom over 101° F; no constant connection of maxima of temperature and of eruption; often normal by second day.	Temperature usually 104°-105° F. from outset for three to four days.
Pulse in proportion to fever.	Pulse in proportion to fever.	Pulse very rapid.
Diarrhœa common during eruption.	Diarrhœa rare.	
Albuminuria not very common.	Albuminuria very rare.	Albuminuria very frequent.
	DESQUAMATION.	
Branny.	Absent; or slight, branny.	In flakes or rolls.

PROGNOSIS.—In nearly all cases the prognosis is entirely good. In some severe local epidemics deaths have taken place. These have usually been the result of complications, but in some instances they seem to have resulted from the depressing effects of the disease itself.

TREATMENT.—*Prophylaxis.*—It is exceedingly difficult to limit the spread of the disease, owing to its great contagiousness and to the fact that this exists before any very distinct evidences of illness are present. Any child attacked ought to be separated from the other members of the family, since we can never know that we may not be about to encounter the disease in a severe form.

After recovery such means of disinfection are required as have been
vised for measles. The duration of the infectiousness is difficult to
termine. Quarantine should certainly last three weeks from the onset
the symptoms.

Treatment of the Attack.—But little treatment ordinarily is required,
what is needed is entirely symptomatic. The patient should be
ned to bed and guarded carefully against cold, in view of the pos-
danger of respiratory complications. Darkening of the room is
ot so often needed as in measles, but may be necessary, and should
rtainly be carried out if there is any weakness of the eyes. A light
t is advisable. A febrifuge or perhaps an expectorant or sedative
ugh mixture may be needed if there is much cough. Antipyrine or
her drugs of this class will rarely be required to reduce temperature.
ll severe symptoms or complications are to be treated as they arise.

DIPHTHERIA.

By WILLIAM HALLOCK PARK, M. D.

DIPHTHERIA is an acute infectious disease caused by a specific micro-organism. This micro-organism usually develops upon the mucous membranes, especially those of the upper respiratory tract, but also occasionally upon other wounded surfaces.

The disease is characterized locally by a grayish exudate or pseudomembrane formed chiefly of fibrin, broken-down epithelium, and leucocytes. The development of the membrane is accompanied by swelling and hyperæmia of the adjacent tissues, and by more or less severe fever, prostration, and other constitutional disturbances.

Both the local lesions and general disturbances are caused by the poisonous action of the absorbed toxins produced by the diphtheria bacilli and the associated bacteria. As it is impossible to obtain a correct knowledge of the etiology, diagnosis, or treatment of diphtheria without a thorough understanding of its bacteriology, this portion of the subject will be very thoroughly considered. Even those physicians who never expect to conduct any bacteriological investigations themselves need to inform themselves fully concerning the facts already established in order that they may form correct opinions as to the value of bacteriological examinations in suspected diphtheria, and the worth and limitations of the use of antitoxin in the prevention and treatment of the disease.

SUCCESSIVE INVESTIGATIONS SHOWING THE SPECIFIC CAUSAL RELATION OF THE DIPHTHERIA BACILLUS OF KLEBS AND LÖFFLER TO DIPHTHERIA.

In the year 1883 bacilli which were very peculiar and striking in appearance were shown by Klebs to be of constant occurrence in the pseudo-membranes from the throats of those dying of true epidemic diphtheria. One year later, Löffler published the results of a very thorough and extensive series of investigations on this subject. He found the bacillus described by Klebs in most, but not all, cases of throat inflammations which had been diagnosticated as diphtheria. He separated these bacilli from the other bacteria present and obtained them in pure culture. When he inoculated these bacilli upon the abraded mucous membrane of susceptible animals, pseudo-membranes were produced, and frequently death followed. If a certain amount of a bouillon culture was injected subcutaneously into guinea-pigs, death was caused with characteristic lesions. Löffler's failure to find the bacilli in every case examined is now explained by the fact that certain varieties of pseudo-membranous inflammation not due to the diphtheria bacillus, such as occur especially in scarlet fever, were then wrongly considered to be true diphtheria.

In 1887 further studies by Löffler added to the proof of the dependence of diphtheria on the diphtheria bacilli. In 1888, D'Espiné found the bacilli in 14 cases of characteristic diphtheria, and proved them to be absent in 24 cases of mild sore throats which, clinically, were believed not to be cases of diphtheria. In the same year the first portion of the results of the very important investigations of Roux and Yersin was published, and the dependence of the disease on the diphtheria bacilli may be considered to have been established. Roux and Yersin found the diphtheria bacilli were present in all characteristic cases, and that these bacilli possessed the cultural and pathogenic qualities of those described by Löffler. They found, too, when the bacilli were inoculated upon the healthy mucous membrane of the trachea of the rabbit, no inflammation followed; but if the inoculation was made on the abraded membrane, phenomena occurred which strikingly resembled those present in membranous laryngitis in man—*i. e.* congestion of the mucous membrane, followed by the formation of a pseudo-membrane, œdematous swelling of the tissues and of the glands of the neck, dyspnœa, stridulous breathing, and asphyxia. Injection of cultures beneath the skin of rabbits and guinea-pigs in sufficient quantity caused their death in from thirty-six hours to five days, the period varying in ratio to the susceptibility of the animal and the number and virulence of the bacteria introduced. The same result followed the injections of filtered cultures, showing that the products formed by the growth of the bacilli were, by themselves, capable of causing the general lesions.

Roux and Yersin were also able to produce in animals characteristic diphtheria paralysis. They produced this in many cases where the inoculated animals did not succumb to a too rapid intoxication. Paralysis commenced in a pigeon three weeks after the inoculation of the pharynx and after all membrane had disappeared and the animal seemed to have completely recovered. In rabbits the paralysis usually commenced in the posterior extremities, and then gradually extended to the whole body, causing death by paralysis of the heart or respiration. In rare instances the muscles of the neck or of the larynx were first paralyzed, and thus characteristic symptoms were caused. The authors conclude: "The occurrence of these paralyses, following the introduction of the bacilli of Klebs and Löffler, completes the resemblance of the experimental disease to the natural malady, and establishes with certainty the specific rule of this bacillus."

Finally, the microscopic changes in the internal organs of animals dying of experimental diphtheria produced by the bacilli have been shown by Welch and Flexner, and by Babes and others, to be essentially the same as those produced by diphtheria in man, and thus a still further proof is afforded of the specific rôle of this bacillus.

The results of the various observations detailed above have since been confirmed by a great number of combined clinical and bacteriological investigations, so that all who have studied the bacteriology of diphtheria would now agree with the following statement made by Welch[1] in an address on diphtheria: "All the conditions have been fulfilled for diph-

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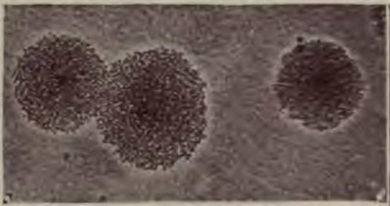
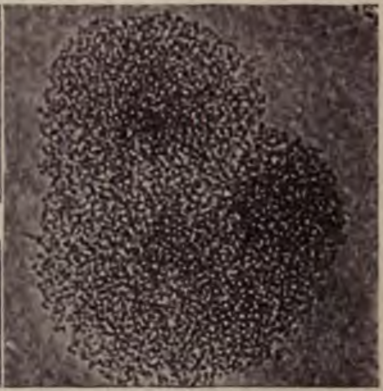
[1] Welch, *Medical News*, May 16, 1891.

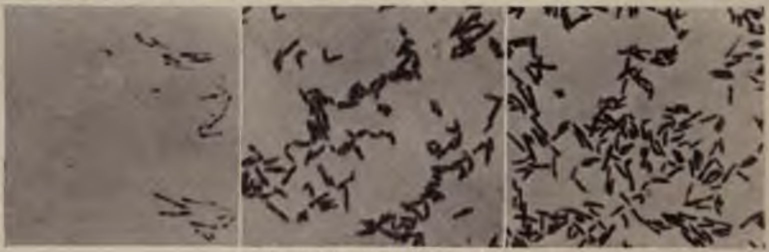
PLATE X.



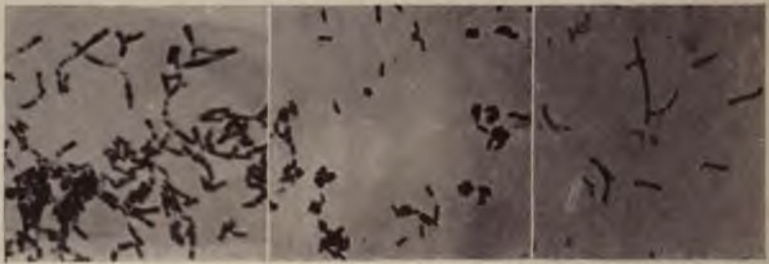
a. Colonies of diphtheria bacilli, × 160.



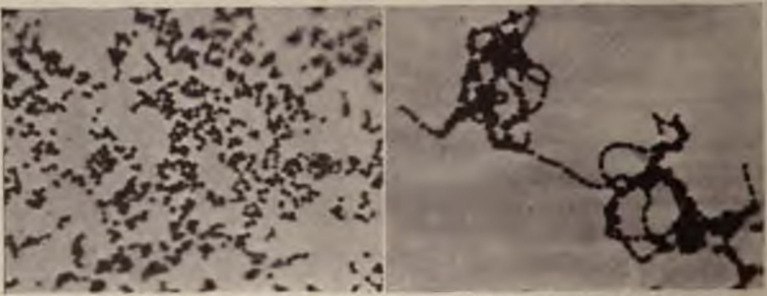
b. Colonies of pseudo-diphtheria bacilli, × 160. *c.* Colonies of diphtheria bacilli, × 240.



d. Diphtheria bacilli, × 1000.



e. Diphtheria bacilli, × 1000. *f.* Pseudo-diphtheria bacilli, × 1000. *g.* Streptococci, × 1000.



h. Streptococci, × 1000. *i.* Streptococci, × 1000.

Diphtheria Bacilli and Streptococci.

theria which are necessary to the most rigid proof of the dependence of an infective disease upon a given micro-organism—viz. the constant presence of this organism in the lesions of the disease, the isolation of the organism in pure culture, the reproduction of the disease by inoculations of pure cultures, and similar distribution of the organism in the experimental and in the natural disease. In view of these facts we must agree with Prudden that we are now justified in saying that the name diphtheria, or at least primary diphtheria, should be applied, and exclusively applied, to that acute infectious disease usually associated with pseudo-membranous affection of the mucous membrane which is primarily caused by the bacillus called the bacillus diphtheriæ of Löffler."

CHARACTERISTICS OF THE LÖFFLER BACILLUS.—*Growth on Blood Serum.*—If we examine the growth of the diphtheria bacillus in pure culture on blood serum, we will find at the end of ten to twelve hours little colonies of bacilli which appear as pearl-gray or whitish-gray slightly raised points. The colonies when separated from each other may increase in forty-eight hours, so that the diameter may be one fourth of an inch. The borders are usually somewhat uneven. Those colonies, lying together, fuse into one mass, especially if the serum is rather moist. During the first twelve hours the colonies of the diphtheria bacilli about equal in size those of the streptococci; but after this time the diphtheria colonies become larger than those of the streptococci, nearly equalling those of the staphylococci. The diphtheria bacilli in their growth never liquefy the blood serum.

When cover-glass preparations made from the blood serum tubes are examined, the diphtheria bacilli are found to possess the following characteristics (Plate X., *d*, *e*):

The diameter of the bacilli varies from 0.3 to 0.8 μ, and the length from 1.5 to 6.5 μ. They occur singly and in pairs, and very infrequently in chains of three or four. The rods are straight or slightly curved, and usually are not uniformly cylindrical throughout their entire length, but are swollen at the ends or pointed at the ends and swollen in the middle portion. Even from the same culture different bacilli differ greatly in their size and shape. The two bacilli of a pair may lie with their long diameter in the same axis or at an obtuse or an acute angle. The bacilli possess no spores, but have in them highly refractile bodies. They stain readily with the ordinary aniline dyes and retain their color after staining by Gram's method. With an alkaline solution of methyl blue, the bacilli, from blood serum especially, and from other media less constantly, stain in an irregular and extremely characteristic way. The bacilli do not stain uniformly. Certain oval bodies situated in the ends or in the central portions stain much more intensely than the rest of the bacillus. Sometimes these highly stained bodies are thicker than the rest of the bacillus; again, they are thinner and surrounded by a more slightly stained portion. The bacilli seem to stain in this peculiar way at a certain period in their growth, so that only a portion of the organisms taken from a culture at any one time will show the characteristic staining. In old cultures it is often difficult to stain the bacilli, and the staining, when it does occur, is frequently not at all characteristic.

Growth on 1 per cent. Alkaline Glycerin Agar, and Method of Obtaining Pure Cultures.—It is frequently desired to obtain the diphtheria bacillus in pure culture. This is most readily accomplished by removing with a platinum needle a portion of the mixed growth of bacteria in a serum tube, and lightly streaking it over the surface of the nutrient agar contained in a Petri dish.

Though the growth of the diphtheria bacilli upon agar is less certain and luxuriant than upon serum, the appearance of the colonies when examined under the microscope is more characteristic.

If the diphtheria colonies develop deep in the substance of the agar, they are usually round or oval, and, as a rule, present no extensions, but if near the surface from one or both sides they spread out an apron-like extension which exceeds in surface area the rest of the colony. When the colonies develop entirely on the surface, they are more or less coarsely granular, are nearly translucent, and usually have a darker centre. The edges are sometimes very jagged, and frequently shade off into a delicate lace-like fringe; at other times the margins are more even and the colonies are nearly circular. With a high power lens the edges show sprouting bacilli (Plate X., *c*). The colonies are gray or grayish white by reflected light, and pure gray with olive tint by transmitted light.

The growth of the diphtheria bacillus upon agar presents certain peculiarities which are of the utmost practical importance. While the bacilli from the majority of cases grow rather feebly, some grow luxuriantly. If a large number of the bacilli from a recent culture are implanted upon a properly prepared agar plate, a certain and fairly vigorous growth will always take place. If, however, the agar is inoculated with the exudate of a throat which contains but few Löffler bacilli, or from a serum tube containing also a growth of other bacteria, no growth whatever of the bacilli may occur, while the tubes of coagulated blood serum inoculated with the same material contain them abundantly. Again, agar prepared from broth made from different specimens of beef, or to which different peptones have been added, varies somewhat as to its suitability for the growth of the bacilli. Because of the uncertainty of obtaining a growth by the inoculation of agar with a few bacilli or with bacilli of diminished vigor, agar is a far less reliable medium than blood serum for use in cultures made for diagnostic purposes, and is, therefore, not to be recommended. All agar should be tested by means of a pure culture of the diphtheria bacillus before being used experimentally.

The agar is prepared by adding 1 per cent. of agar to the required quantity of broth. The broth is prepared in the same way as that used in the blood serum mixture, except that it contains no glucose. The agar must be thoroughly dissolved in the broth, and to accomplish this in an ordinary Arnold sterilizer it is necessary to boil the mixture for from three to six hours. Sufficient alkali must be added to make the agar slightly but distinctly alkaline. Many advise that before final sterilization 5 per cent. glycerin be added. The bouillon agar sterilized on three successive days may be kept for many months in litre flasks.

Growth in Broth.—All the varieties of the Löffler bacillus experimented with have grown in slightly alkaline broth with or without the addition of 1 per cent. glucose. The characteristic growth is one showing fine grains. These deposit along the sides and bottom of the tube, leaving the broth nearly clear. In some cultures for twenty-four or forty-eight hours there is a more or less diffuse cloudiness, and, exceptionally, a film forms over the surface of the broth. On shaking the tube this film breaks up and slowly sinks to the bottom. As a rule, the bacilli cause the alkaline broth to become acid, or at least distinctly less alkaline, within forty-eight hours. As a rule, within a week the acid reaction changes again to the alkaline. This may occur in forty-eight hours or, exceptionally, not at all. These differences are due largely to the character of the meat from which the broth is made, especially upon the amount of glucose contained.

Animal Inoculations as a Test of Virulence.—Animal experiments form the only reliable method of determining with certainty the virulence of the diphtheria bacillus. For this purpose alkaline broth cultures of forty-eight hours' growth should be used for the subcutaneous inoculation of guinea-pigs. The amount injected may vary from $\frac{1}{4}$ to $\frac{1}{2}$ per cent. of the body weight of the animal inoculated. In the great majority of cases, when the bacilli are virulent, this amount causes death within seventy-two hours. Some bacilli are so virulent that $\frac{1}{100}$ of of this amount causes death. In the autopsy the characteristic lesions described by Löffler are found—namely, at the seat of inoculation there is a grayish focus surrounded by an area of congestion ; the subcutaneous tissues for an extensive area around are congested, and at times very œdematous; the adjacent lymph nodes are swollen, and the serous cavities—especially the pleura—frequently contain an excess of fluid, usually clear, but at times turbid ; the lungs are usually congested. If the organs are subjected to microscopical examination, the lesions described by Welch and Flexner, Babes, and others are found. There are numerous smaller and larger masses of necrotic cells, which are permeated by leucocytes. The heart and the voluntary muscular fibres usually show degenerative changes. The number of leucocytes in the blood is increased. From the area surrounding the point of injection virulent bacilli may be obtained, but in distant areas and organs they are only occasionally found.

Bacilli which in cultures and in animal experiments have shown themselves to be characteristic may be regarded as certainly true diphtheria bacilli, and as capable of producing diphtheria in man under favorable conditions.

THE PREPARATION OF LÖFFLER'S BLOOD SERUM MIXTURES; THE MEDIA USED FOR MAKING CULTURES FOR DIAGNOSTIC PURPOSES.

Collection of the Blood Serum and its Preparation for Use in Cultures.—A covered glass jar, which has been thoroughly cleansed with hot water, is taken to the slaughter-house and filled with freshly shed blood from a calf or sheep. The blood is received directly in the jar as it spurts from the cut in the throat of the animal. After wiping the edge of the jar, it is covered with the lid and set aside where it may stand quietly until the blood has thoroughly clotted. It is then placed in a cool place. It is well to inspect the blood in the jar after it has been standing a few hours, and, if the clot is found adhering to the sides, to separate it by a rod. The blood is allowed to remain twenty-four hours on

and then the serum which surrounds the clot is siphoned off by a
r tube and mixed with one third its quantity of nutrient beef
to which 1 per cent. glucose has been added. This constitutes
öffler blood serum mixture. The broth used to mix with the
is prepared as follows: One pound of finely chopped lean beef is
d to soak in one litre of water in a cool place for twelve to twenty-
ours. The meat and fluid are now dumped into a cheese-cloth or
and the fluid squeezed out. To this solution 1 per cent. of peptone,
r cent. of glucose, and 0.5 per cent. of common salt are added. It
ell to test the reaction of the mixture, and, if it is found to be acid,
ender it neutral by adding a few drops of a solution of caustic soda
carbonate of soda. The whole is now boiled for half an hour and
tered through sterilized absorbent cotton or filter paper. If the broth
to be kept, it should be placed i [illegible] sks and sterilized. The Löffler
ood serum mixture when ready [illegible] poured into tubes, which should be
about four inches in length and two thirds of an inch in diameter.
These tubes should first be plugged with cotton and sterilized by dry heat at 150° C. for one hour. Care should be taken in filling the tubes to avoid the formation of air bubbles, as they leave a permanently uneven surface when the serum has been coagulated by heat. To prevent this, the end of the pipette or funnel which contains the serum should be inserted well into the test tube. About 2 c.c. are sufficient for each tube. The tubes, having been filled, are now to be coagulated and sterilized. They are placed at the proper angle, and then kept for two hours at a temperature just below the boiling point. For this purpose a Koch serum coagulator or a double boiler serves best, though a steam sterilizer will suffice. If the latter is used, a wire frame must be arranged to hold the tubes at the proper inclination, and the degree of heat must be carefully watched, as otherwise the temperature may go too high, the serum be actually boiled, and the culture medium, becoming full of bubbles, thus spoiled. After sterilization by this process the tubes containing the sterile, solidified blood serum can be placed in covered tin boxes and kept for months. The serum thus prepared is quite opaque and firm. A mixture of blood cells renders the serum darker, but it is not less useful.

The Swab for Inoculating Culture Tubes.—The swab to inoculate the serum is made as follows: A stiff, thin steel rod, like a knitting needle, six inches in length, is roughened at one end by a few blows of a hammer, and about this end a little absorbent cotton is firmly wound. Each swab is then placed in a separate glass tube, and the mouths of the tubes are plugged with cotton. The tubes and rods are then sterilized by dry heat at about 150° C. for one hour, and stored for future use. These cotton swabs have proved much more serviceable for making inoculations than platinum wire needles, especially in young children and in laryngeal cases. It is easier to use the cotton swab in such cases, and it gathers up so much more material for the inoculation that it has seemed more reliable.

For convenience and safety in transportation a "culture outfit" may be devised, which consists of a small wooden box containing a tube of blood serum, a tube holding a swab, and a record blank. These "culture outfits" may be carried or sent by messenger or express to any place desired, or kept by the Health Board at stations scattered throughout the cities for the free use of physicians.

Directions for Inoculating Culture Tubes with the Exudate in Cases of Suspected Diphtheria.—The patient should be placed in a good light and, if a child, properly held. The swab is removed from its tube, and while the tongue is depressed with a spoon it is passed into the pharynx (if possible without touching the tongue), and is rubbed gently but firmly against any visible membrane on the tonsils or in the pharynx, and then, without laying the swab down, it is immediately inserted in the blood serum tube, and the portion which has been previously in contact with the exudate is rubbed a number of times back and forth over the whole surface of the serum. This should be thoroughly done, but it is to be gently done, so as not to break the surface of the serum. The swab is replaced in its tube, and both tubes, their cotton plugs having been inserted, are returned to the box and sent to the collecting station.

Where there is no visible membrane (it may be present in the nose or pharynx) the swab should be thoroughly rubbed over the mucous membrane of the pharynx and tonsils, and in nasal cases, when possible, a culture should also be made from the nose. In little children care should be taken not to use the swab when the throat contains food or vomited matter, as then the bacterial examination is rendered more difficult. Under no conditions should any attempt be made to collect the material shortly after the application of disinfectants (especially solutions of corrosive sublimate) to the throat. If any of these instructions have not been carried out, the fact should be carefully noted on a record blank.

The Examination of Cultures.—The culture tubes which have been inoculated as described above are kept in an incubator at 37° C. for twelve hours, and are then ready for examination. On inspection it will be seen that the surface of the blood serum is dotted with very numerous colonies, which are just visible. No diagnosis can be made from simple inspection (if, however, the serum is found liquefied or shows other evidences of contamination, the examination will probably be unsatisfactory). A platinum needle is now inserted in the tube, and quite a large number of colonies are swept with it from the surface of the culture medium. The bacteria adherent to the needle are washed off in the drop of water previously placed on the cover-glass and smeared over its surface. The bacteria on the glass are then allowed to dry in the air. The cover-glass is then passed quickly through the flame of a Bunsen burner or alcohol lamp three times in the usual way, covered with a few drops of Löffler's solution of alkaline methyl blue, and left without heating for ten minutes. It is then rinsed off in clean water, dried, and mounted in balsam.

In the great majority of cases one of two pictures will be seen with the $\frac{1}{12}$ inch oil immersion lens—either an enormous number of characteristic Löffler bacilli with a moderate number of cocci, or a pure culture of cocci, mostly in pairs or short chains (Plate X., *h*). In a few cases there will be an approximately even mixture of Löffler bacilli and cocci, and in others a great excess of cocci. Besides these, there will be occasionally met preparations in which, with the cocci, there are ngled bacilli more or less resembling the Löffler bacilli. These bacilli, ich are pseudo-diphtheria bacilli (Plate X., *f*), are especially frequent cultures from the nose.

In not more than one case in twenty will there be any serious diffi- in making the diagnosis if the serum tube has been properly culated. In such a case another culture must be made or the case ated upon its clinical history alone.

The Direct Microscopical Examination of the Exudate.—An imme- ite diagnosis, without the use of cultures, is usually possible to an ex- t from a microscopical examination of the exudate. This is made smearing a cover-glass with a little exudate from the swab, drying, ining, and examining it microscopically. This examination, however, s much more difficult, and the results more uncertain, than when the covers are prepared from cultures. The bacilli from the membrane are often less typical in appearance than those found in cultures, and they are mixed with fibrin, pus, and epithelial cells. They may also be very few in number in the parts reached by the swab, or bacilli may be met which closely resemble the Löffler bacilli in appearance, but which differ greatly in growth and in other characteristics. When in a smear containing mostly cocci a few of these doubtful bacilli are present, it is impossible either to certainly exclude or make the diagnosis of diphtheria. Although in certain cases this immediate examination may be of the greatest value, it is not a method suitable for general use when cultures are possible.

Having considered the technique, it is well to review carefully and without bias the question as to how much reliance can be placed on the bacteriological diagnosis made from the examination of a culture inoculated with the exudations in the throat of a case of suspected diphtheria.

From time to time, in order to test the results of examinations and to make the liability to error as slight as possible, I adopted the following plan:

A certain number of cases in which the cultures yielded no diphtheria bacilli were turned over to specially trained Health Board inspectors, who made a second culture, and followed up the case during the illness and for some time even after its recovery.

By means of the information thus obtained we were able more and more surely to decide how far we could base an absolute diagnosis on a culture, especially when made by others. It was found that many physicians, as well as the Health Department inspectors, gradually became so skilled in making inoculations that it was possible to rely almost certainly on the results obtained from the examination of their cultures, while, on the other hand, caution was necessary in accepting the inoculations of others, and in such cases a second culture was requested.

After a two years' trial, the following conclusions have been arrived at:

The examination by a competent bacteriologist of the bacterial growth in a blood serum tube which has been properly inoculated and kept for fourteen hours at the body temperature can be thoroughly relied on in cases where there is visible membrane in the throat if the culture is made during the period in which the membrane is forming, and no antiseptic, especially no mercurial solution, has lately been applied.

In cases in which the disease is confined to the larynx or bronchi, and where, therefore, there is no visible exudate against which the swab can be rubbed, surprisingly accurate results can be obtained from the examination of cultures, but in a certain proportion of cases no diphtheria bacilli will be found in the first culture, and yet will be abundantly present in later ones, the bacilli having probably been coughed up more freely as the disease progressed. I believe, therefore, that absolute reliance for a diagnosis cannot be placed on a negative result in cultures from the pharynx in purely laryngeal cases.

In nasal diphtheria a negative result may be obtained from a culture made from the throat, and yet the bacilli be found in cultures from the nose.

In making a diagnosis from a culture it is essential to know the duration of the disease in the case from which it was made, because, although bacilli may remain present and alive in some throats for many weeks, it is, nevertheless, important to remember they may vanish early and suddenly, and that, therefore, the cultures cannot be certainly relied on after the membrane begins to disappear.

The use of antiseptics shortly before making the inoculation of a culture tube may render the culture useless for diagnosis. It has been found in a few instances that a culture made from a case of diphtheria shortly after a thorough irrigation with a 1:4000 solution of bichloride of mercury gave no diphtheria bacilli, though one made just before and one made some time later gave them abundantly. It is a curious fact that under such circumstances a vigorous growth of other organisms may take place.

The above conclusions are true only when the inoculations have been properly made, and, in judging cultures received from physicians in general, the greatest care must be taken. Some cultures are made carelessly, and some evidently without taking the pains to even read the instructions, which should always accompany the outfit, or to glance at the condition of the coagulated serum in the tube. If, therefore, when no diphtheria bacilli are found the bacterial growth is scanty, the media dry or contaminated, or the inoculation in any way faulty, the case must be referred back for another culture. The second culture in these cases not infrequently contains the bacilli when the first did not.

The absence of bacilli in a culture proves the case to be one of false diphtheria only when it has been possible to make it under the proper conditions.

A most important practical question is the following: If, in cultures, bacilli are found which possess the shape, size, and staining characteristics of the diphtheria bacillus, can they, without further cultural or animal experiments, be considered as virulent diphtheria bacilli?

Since it is the custom of many, following the example of the New York City Health Department, to make a bacteriological diagnosis in suspected cases of diphtheria from the examination of the growth on the original blood serum tube without waiting for further cultural or animal experiments, it is of the greatest practical importance to ascertain to what extent bacilli appearing upon the serum in every way characteristic of the diphtheria bacilli can be assumed to be virulent.

To test the virulence of bacilli, four days at least are required, for before inoculating it is necessary to obtain them in pure culture, for otherwise it would be impossible to determine whether the changes produced in the inoculated animal were due to the supposed diphtheria bacilli or to other micro-organisms injected with them. It is further necessary to grow the bacilli in proper media, and to inoculate susceptible animals at a period when the growth of the bacilli in the media has reached its maximum. It is only when these precautions have been followed that accurate results will be obtained. The present almost uniform practice is to inoculate half-grown guinea-pigs with from 0.25 to 0.5 per cent. of their body weight of a twenty-four or forty-eight hours' culture of the bacilli grown at 37° C. in simple nutrient or glucose alkaline broth. It is important to remember that it is not safe to decide, because the growth derived from one bacillus is not virulent, that all the bacilli from that throat are not virulent. The cultures from several bacilli must be tried. The majority of those who have inoculated bacilli derived from pseudo-membranes and possessing the characteristics of the Löffler bacilli have found, as Löffler did, that they were always virulent. The researches of Hofmann, Beck, and others, however, showing that in a certain number of healthy throats there were bacilli which closely resembled the Löffler bacillus, and yet were not virulent, stimulated others to subject the bacilli from large numbers of cases of suspected diphtheria to the test of animal inoculation.

In 1890, Roux and Yersin published the results of some examinations as to the virulence of the bacilli obtained from 100 cases of diphtheria: 55 of these were fatal cases, and in all of them virulent bacilli were found, although in a few, together with many virulent bacilli, there were a few non-virulent ones. Among the 45 cases which recovered many were very mild, and in 10 of them they found no bacilli of sufficient virulence to cause the death of guinea-pigs when injected in moderate amount. From all of them, however, they obtained bacilli capable of causing inflammation in the guinea-pig at the point of injection. This varied from slight, transient œdema to extensive necrosis. From further experiments they proved similar bacilli were capable under proper conditions of regaining their virulence. They further showed that, in these milder cases, among many non-virulent or slightly virulent bacilli there were usually a few virulent ones; therefore they believed that in most of these 10 cases fully virulent bacilli may have been present in the throat with the slightly virulent ones which by chance were used for the inoculations.

Virulence of the Bacilli found in Ten Cases of Throat Inflammation of such a Character as to Arouse a Suspicion of Diphtheria.

Severity.	Weight of guinea-pig, gms.	Amount of culture injected, c.c.	Duration of life after inoculation.	Persistence of Löffler bacillus after recovery of patient.
1. Mild case	390	1.33	40 hours	38–41 days.
2. Mild case; adult; never in bed	210	0.5	50 hours	44 days.
3. Removed to Diphtheria Hospital; severe case	220	0.5	40 hours.	
4 Rather mild case	620	3.33	25 hours	42 days.
5. Very mild case	479	2	No reaction.	20–24 days.
6. Fatal case; croup	675	1.5	40 hours.	
7 Fairly severe case, followed by measles	443	1.33	40 hours	15–23 days.
8. Moderately severe case	435	1.33	4 days	15–19 days.
9. Very mild case	500	1.66	40 hours.	
10. Contracted from a mild case; no membrane present	250	1	40 hours.	

In order to determine the virulence of the bacilli obtained in the ordinary routine examinations from suspected cases of diphtheria blood serum cultures from 40 cases were selected in which bacilli were found having the characteristic appearance of the virulent diphtheria bacilli. The cultures tested were selected before any information was possessed of the severity of the cases from which they were obtained, and were used for experiments on animals. The table given on the preceding page presents average examples of the cases.

We found that the bacilli obtained from 40 cases of suspected diphtheria, two thirds of which were mild, proved in every case except 1 to be virulent, and in all but 3 fully so. If these results are considered in connection with those obtained by other American and by European observers, we must conclude that for diagnostic purposes all bacilli found in throat inflammations of cases suspected to be diphtheria, which possess the morphological and cultural characteristics of the Löffler bacilli, must be regarded as virulent, unless animal inoculations prove otherwise. Further, it should be remembered (as shown by Roux and Yersin, and as confirmed by others and by ourselves) that the absence of virulence in a culture derived from one bacillus is not sufficient to prove that cultures from other bacilli from the same case would not be virulent. This may have been true in the only case out of the 40 in which virulent bacilli were not found.

In 3 of the above cases the cultures from the first colony selected were not virulent, while from others they were fully so.

If a piece of membrane be removed from the throat during the period of invasion of diphtheria and examined microscopically or by cultures, the presence of abundant diphtheria bacilli will be noted. If, a few days later, when the membrane has begun to loosen, another bit be examined, the diphtheria bacilli will be found to be partly or at times wholly replaced by other micro-organisms, mostly cocci. If, several days later, after the complete disappearance of the membrane, cultures be made from the mucus of the throat, it will be found the bacilli of diphtheria in many of the cases will have disappeared from the throat. This rule is not, however, without many exceptions, for it will be frequently found, days after the complete disappearance of the membrane and after the return of the throat to a healthy condition, that fully virulent bacilli linger in the throat.

In order to test the virulence of the bacilli in the throats of convalescent cases, they were obtained in pure culture from a large number of healthy throats in convalescent diphtheria cases and used for the inoculation of the guinea-pigs. The table of selected cases (see next page) gives the average results of these experiments.

In each case, in testing the virulence of the bacilli derived from it, we employed the last culture or the next to the last culture made from it in which the bacilli were found to be present. The results in these cases tested, as well as in those before recorded by others, prove conclusively that the bacilli, which in a certain proportion of cases persist in the throat after an attack of diphtheria, are always virulent for some time. In the exceptional cases in which the bacilli persist for a very long time it is found they occasionally lose their virulence a few days before their final disappearance, while in other cases they retain their ulence to the end. That the cases themselves are not so liable to ead diphtheria is probably because of the relatively small number of illi present in convalescent throats as compared with the number d in those showing the lesions of diphtheria.

	Severity of the diphtheria in the case.	The bacilli tested had persisted after recovery for—	Virulence.		
			Weight guinea-pig, gms.	Amount injected, c.c.	Life of guinea-pig after injection.
1	Mild case	10 days . . .	250	0.5	8 days.
2	Very mild case	12 " . . .	440	1.5	40 hours.
3	Mild case	33 " . . .	226	1.00	Extensive necrosis with final recovery.
4	Severe case	18 " . . .	229	1.00	9 days.
5	Very mild case	25 " . . .	505	1.66	40 hours.
6	Fairly severe case	26 " . . .	347	1.33	5 days.
7	Mild case	50 " . . .	410	3.00	2 "

The Pseudo- and Non-virulent Diphtheria Bacillus.—Since the general adoption of bacteriological examinations for purposes of diagnosis in diphtheria the characteristics of the non-virulent bacilli and the frequency with which they occur have had added to their scientific a very practical interest.

In 1888, Hofmann published the results of the bacteriological examinations of a number of diseased and healthy throats, which for a time threw doubt on the specific character of the Löffler diphtheria bacillus. Further research has largely dispelled the confusion which his discoveries seemed to make.

Hofmann's results were similar to those of Löffler, in that he found the virulent bacillus in all of 8 cases of true diphtheria, but in further search he was surprised to find in the throats of 26 out of 45 persons, none of whom was suffering from diphtheria, a bacillus which very closely resembled the Löffler bacillus. The bacilli from a number of these healthy throats were obtained in pure culture and inoculated into animals. The majority had no virulence whatever. The bacilli from the different cases varied somewhat in their characteristics. Some in appearance, manner of staining, and growth on media seemed identical with the Löffler bacillus, while others presented slight but constant differences. Between the extremes were many gradations.

Those bacilli which did not possess all the characteristics of the virulent bacillus differed in the following respects: They were shorter, thicker, and more uniform in size. On agar they grew in whiter and thicker colonies, whose circumference was more circular and less notched. They also grew at a lower temperature than the virulent bacilli (20° to 22° C.).

Hofmann was undecided whether all of these bacilli were really Löffler diphtheria bacilli which had lost their virulence, or whether they were a different species of bacteria and of a saprophytic nature. He was also undecided whether, even among these non-virulent bacilli, there might not be included different species.

Roux and Yersin found in a hospital for children in Paris, where cases of diphtheria occurred from time to time, that 15 out of 45 children contained in their healthy throats non-virulent bacilli resembling the

Löffler bacillus. In a French village where no diphtheria had been present for a long time they made cultures from the healthy throats of 59 children living in a school. In 26 of these non-virulent bacilli were found. In an examination of the throats of 10 attendants in a diphtheria hospital non-virulent bacilli were found once. Thus in 114 healthy throats the non-virulent bacilli were found 42 times. In all of these throats the bacilli were present in very small numbers.

The bacilli found, when studied in pure culture, differed somewhat from each other. The majority were identical in all their characteristics with the Löffler bacillus, except as to their lack of virulence. The minority resembled those described by Hofmann. Roux and Yersin regarded the occasional slight differences in growth, shape, and staining as too slight and inconstant to distinguish the virulent from the non-virulent bacilli. Animal experiments alone sufficed to determine the question of virulence, and they regarded as arbitrary a division founded on the reaction of the guinea-pig to inoculation, since they found that bacilli from cases of diphtheria may possess every degree of virulence, from those which cause death within twenty-four hours to those which caused only a temporary œdema. With such variations it is a difficult matter to determine what should be the proper line of division between the virulent and the non-virulent bacilli.

To fully prove that these bacilli belong to the same species they believe it is necessary to derive non-virulent bacilli from the virulent ones, and to give virulence to those entirely lacking it.

They found it was possible to produce an attenuation of the virulence of the bacilli in a number of ways. They also found it possible to greatly increase the virulence of bacilli by injecting them together with a virulent culture of the streptococcus of erysipelas; but were unable, on the other hand, to give back virulence to those bacilli which had been completely robbed of their virulence by the above methods, or to those which had no virulence when obtained from the throat.

If we now turn to the work of Escherich, we find results which tend to show that the virulent and some of the non-virulent bacilli are different species of bacteria. He found the bacilli from every case of diphtheria examined to be fully virulent, and in a few cases, where he obtained characteristic bacilli from the healthy throats of persons exposed to diphtheria, he found them also to be virulent.

Escherich did indeed find in a moderate number of throats of persons not suffering from diphtheria bacilli similar to those described by Hofmann. Thus in Munich he found this non-virulent bacillus in 2 throats out of 70, and in Grez in 11 out of 250, or 13 times in 320 cases. These bacilli, however, all possessed certain cultural and morphological characteristics which were sufficient to separate them from the virulent bacilli. They were, as in some described by Hofmann, plumper and shorter than the Löffler bacilli and more uniform in size. He noticed two new points of difference which seemed to him important. The non-virulent or pseudo-diphtheria bacilli, when spread on a cover-glass, lie in parallel rows, while the virulent diphtheria bacilli lie at every angle and the most varied positions. The second difference was still more marked. He found, as had all others who had noticed this point, that the virulent bacilli in their growth in neutral or slightly line bouillon changed the reaction of the bouillon to acid in the rse of forty-eight hours. The amount of acid formed differed in rent cultures and had no relation to the degree of virulence. He noticed that the substance produced during the growth of the o-diphtheria bacilli always made the bouillon more alkaline instead d. Therefore, if at the end of forty-eight hours litmus was added he different bouillon cultures, it turned red in the virulent ones and e in the pseudo-diphtheritic non-virulent ones. It should be noticed t this difference in reaction was not found by Roux and Yersin in cultures of the non-virulent bacilli tested by them.

Escherich, in conclusion, states his position as follows: "Since we ve found constant cultural differences between the true and the eudo-diphtheria bacilli, we can give the pseudo-diphtheria bacilli no agnostic value."

If we review the remaining literature of this subject, we find some investigators have been led by their results to adopt views similar to those of Roux and Yersin, others to those of Escherich, and still others have been forced to content themselves with the position of Hofmann—viz. that we are not in a position to affirm whether all these bacilli are of one or of different species of bacteria.

The relationship between these bacilli is not only a matter of great interest, but has also been one of great practical importance in bacteriological examination carried on for purposes of diagnosis.

In order to study these various bacilli, especially the non-virulent forms, and to clear up, if possible, some of the questions connected with their classification, cultures were made upon blood serum from 330 healthy throats.

When any of the varieties of bacilli described above were discovered in the cultures, they were isolated, and in the great majority of cases tested as to their virulence on guinea-pigs. In these examinations I had the help of Mr. Alfred Beebe. The results are given in the tables below.

Results of Cultures made from the Throats of Healthy Persons where there had been no History obtained of Direct Contact with Diphtheria.

From where.	Total cases.	Virulent characteristic diphtheria bacilli.	Non-virulent characteristic diphtheria bacilli.	Non-virulent pseudo-diphtheria bacilli.
	Nos.			
New York Dispensary, by Dr. J. H. Huddleston	1 to 151	3	12	21
Northern Dispensary	152 to 163			
Vanderbilt Clinic	164 to 189	. . .	2	2
Throughout the city of New York	190 to 193	. . .	4	
College of Physicians and Surgeons—Students	194 to 242	. .	2	3
New York Foundling Hospital Dispensary .	243 to 257	. . .	. . .	1
Orthopædic Hospital (through kindness of Dr. Chappell).				
Female ward	258 to 267	. . .	3	
Male ward	268 to 275			
New York Foundling Hospital, by Dr. Adams	276 to 330	5	1	
Totals	330	8	24	27

The bacilli found may be divided into three groups:

(1) Bacilli identical with the Löffler diphtheria bacillus in growth, producing acid in bouillon, but having no virulence.

(2) Bacilli not having all the characteristics of the Löffler bacillus in growth, producing alkali in bouillon and having no virulence.

(3) Virulent Löffler diphtheria bacilli, characteristic in growth, producing acid in bouillon.

Two hundred and eighty of the 330 healthy persons from whose throats cultures were made were children under twelve, while 50 were adults. In 24 of these characteristic but non-virulent bacilli were found, and in only 9 of the 24 were there present noticeable pathological changes in the throat, such as enlarged tonsils. The bacilli persisted in 4 of the throats for four weeks, in 1 for three weeks, in 3 for two weeks, and in some of the others for shorter periods.

These bacilli were abundant in the primary cultures from 17 cases, and present in small numbers only in the cultures from 7.

Upon blood serum the bacilli grew in a manner characteristic of the Löffler bacillus.

Column III. of the table shows that in 27 cases bacilli were found corresponding to those described by Hofmann. These were smaller, shorter, thicker, and more uniform in size than the characteristic Löffler bacilli, and always formed alkali in their growth in broth, but no acid. On agar they grow as the less characteristic varieties of the virulent bacilli. These bacilli were never virulent in animals. Guinea-pigs were inoculated with large amounts ($\frac{1}{2}$ to 1 per. cent. of their weight) of broth cultures of bacilli, obtained from 8 cases, without showing any reaction.

As is shown in Column I. of the table, virulent diphtheria bacilli were found in 8 of the 330 cases. They were, in all probability, derived from mild cases of unrecognized diphtheria or from healthy children who were carrying the bacilli in their throats.

Cultures from a number of pseudo-diphtheria bacilli were carried through a series of generations without losing their characteristics, thus differing from most acid-producing bacilli, which after a little cultivation usually show the characteristic appearances of diphtheria bacilli.

Whether or not these pseudo-diphtheria bacilli are descendants of the virulent or non-virulent diphtheria bacilli is perhaps a question impossible to answer. They have at present certain well defined differences which seem to be fixed.

The Frequency with which Virulent Diphtheria Bacilli are Present in the Throats of Healthy Persons who have been Brought in Contact with Diphtheria.—The search for the origin of obscure cases of diphtheria has revealed the fact that it is possible for the human throat to become the habitat of the virulent Löffler bacillus without any visible lesions resulting. Thus, Löffler found the virulent bacillus once, Fränkel twice, and Escherich found it in several cases. In one of Escherich's cases the history is so significant as to be worth repeating. It was noticed that among the children coming under the care of a certain apparently healthy nurse a number of cases of diphtheria were developing. A bacteriological examination being made, her throat was found to contain very numerous virulent diphtheria bacilli. These remained present and virulent for weeks. A similar and interesting case is reported by Feer. In a diphtheria epidemic occurring in a hospital ward, due to a single infection, the throats of 7 children became infected. The infection caused fatal diphtheria in 4, an acute angina without membrane in 2, and no sympoms whatever in 1. In all of these the bacilli were abundant and ually virulent. Many similar examples have been met with in New ork City.

A very interesting investigation has been carried on to determine ow frequently the throats of healthy children become infected in milies where one is sick with diphtheria, and where little or no isolaion is possible.

As will be seen by the following tables, the throats of the healthy children of 14 families, in which one or more of the other members had diphtheria, were examined. There were, in all, 48 healthy children. In 50 per cent. of these diphtheria bacilli were found; 40 per cent. of these developed later, to a greater or less extent, the lesions of diphtheria. In considering the high percentage of cases in which this virulent Löffler bacillus was found, it must be remembered that in these families the conditions were the best possible for the transmission of the contagium.

In numerous instances cultures have been made from the throats of healthy children in families where the diphtheria case was well isolated; in such cases the bacilli have been found in less than 10 per cent. of the children. Even here contact with the sick was allowed up to the time the disease was diagnosticated.

Family.	Number of cases examined aside from the original case of diphtheria.	Löffler bacilli.		Remarks.
		Found in	Not found in	
A.	1	. . .	1	Isolation partial.
B.	3	3	. . .	No isolation; all three cases subsequently developed diphtheria.
C.	2	1	1	No isolation.
D.	1	1	. . .	"
E.	3	1	2	"
F.	4	1	3	Isolation partial.
G.	5	3	2	"
H.	4	3	1	No isolation.
I.	4	1	3	Isolation partial.
J.	8	3	5	"
K.	4	1	3	"
L.	3	2	1	"
M.	5	3	2	"
N.	1	1	. . .	No isolation.
14	48	24	24	

Of the above cultures in which the Löffler bacilli were found, in 6 the virulence was tested in the usual way. The results are stated in the following table:

Family No.	Case No.	Amount bouillon culture inoculated.	Weight guinea-pig, gms.	Virulence.	Clinical history.
B.	1	1.33 c.c.	337	Died in 40 hours.	Developed fatal diphtheria one day after culture was taken.
G.	2	1 "	205	Died in 44 hours.	Developed tonsillar diphtheria two days after culture was taken.
H.	3	1.33 "	202	Died in 48 hours.	No subsequent development of diphtheria.
K.	4	1.33 "	300	Died in 40 hours.	" " " "
M.	5	1.66 "	490	Died in 40 hours.	" " " "
N.	6	1 "	250	Died in 40 hours.	" " " "

It may be interesting to detail here 2 instances out of many observed in which the virulent bacilli of diphtheria derived from healthy throats have been the cause of diphtheria in others:

1. A child was admitted into a hospital ward in an anæmic condition and with a chronic coryza. Five days later 4 children in his neighborhood developed diphtheria; 2 of these died. In seeking the cause of the diphtheria suspicion was directed to the child by a slight nasal discharge. Bacteriological examination showed that this secretion contained many diphtheria bacilli. On further examination it was found the child came from a family in which three weeks before there had been a case of diphtheria.

2. In a family of 8 children 1 child sickened with diphtheria and a second child, a baby, was sent to a neighbor. The next day cultures showed this baby, as well as 2 of the other children, all of whom were apparently healthy, to be infected with diphtheria bacilli. The 3 apparently healthy, but infected, children, as well as the sick one, were at once quarantined, but already 1 of the family to which the baby had been sent had contracted diphtheria from it.

The practical value of bacteriological examinations of the throats of healthy children in families where isolation has not been carried out in the first days is further shown by the fact that those children in whom the bacilli are found are extremely apt to develop diphtheria in the course of a few days, when no cleansing treatment is adopted, while they seem much less liable to do so if kept under treatment or immunized with antitoxins.

The detection of the virulent bacilli in throats prevents the dissemination of diphtheria by allowing us to isolate those infected.

A very striking instance of this was the following: In a family of 4 children 1 was sick with diphtheria. The Department inspector found 3 other children in the same bed with the sick child, who was constantly spitting upon and soiling the bedclothes. He made cultures from these 3 children, whose throats appeared healthy, as well as from the sick one; all contained abundant characteristic Löffler bacilli (these were later shown to be virulent by the inoculation of guinea-pigs). When the inspector visited the same family three days later he found 2 of the previously healthy children had meanwhile sickened and died, and that the third was severely ill. This child finally recovered.

From the observation detailed above we cannot escape the conclusion that all members of an infected household should be regarded as under suspicion, and in those cases where isolation is not enforced the healthy as well as the sick should be prevented from mingling with others until cultures from the throat have shown the absence of bacilli or a sufficient lapse of time gives the presumption that they are not carriers of the contagium.

Summary and Conclusions on Diphtheria Bacilli in Healthy Throats.—It has been shown that children, and to a less extent adults, who are brought in direct contact with true cases of diphtheria very often receive the diphtheria bacilli into their throats, and that these bacilli may persist and develop in these throats for days or weeks. In some cases we have found that true diphtheria followed the appearance of the bacilli in the respiratory passages, while in others no disease developed, though they might be the source of diphtheria in others. The examination of the throats of 330 healthy persons dwelling in New York tenements in whom no contact with diphtheria was known revealed the presence of ent cilli in but 8 persons, 2 of whom later developed diph- ia.

We must conclude, then, that virulent diphtheria bacilli are to be nd in the throats of a small proportion of healthy persons throughout ies where diphtheria prevails, and that they have been derived directly from diphtheria cases or from those who have been in tact with them. The examinations of the throats of the 330 healthy sons showed that in 24 bacilli existed in every way identical with the ffler bacillus, except that they were not virulent in animals. As some the bacilli in cases of true diphtheria are known to gradually lose ir virulence, and as this loss can be caused artificially, it seems that ese bacilli, characteristic except as to virulence, should be regarded as rue diphtheria bacilli which have lost it. They are probably incapable of causing diphtheria.

The examination of the same throats showed that in 27 there were bacilli present which were so uniform in their peculiarities, as to staining, size, shape, and the production of an alkali instead of an acid, that there seems to us to be even more reason to separate them from the diphtheria bacillus than there is, for example, to separate the colon bacillus from that of typhoid.

We have never found bacilli possessing these peculiarities to be virulent, nor have they appeared to have any connection with diphtheria. It seems to us that to these bacilli alone the name pseudo-diphtheria bacillus should be given.

The Persistence of Bacilli in the Throats of Convalescent Cases.—The length of time elapsing between the inception of the disease and the date on which a culture showed the absence of the Klebs-Löffler bacillus from the throat of the patient was tabulated for 1736 cases.

In many of the cases cultures were made at infrequent intervals, and the bacilli may therefore have disappeared at an earlier period than that recorded. In cases where cultures show the disappearance of the bacilli on the fourteenth day or over, the average interval between these cultures and the last culture showing the presence of the bacilli is probably about eight days.

The tabulation is as follows:

Time from inception of disease bacilli disappeared,	56th day.	49th day.	42d day.	35th day.
Number of cases	1721	1706	1676	1622
Per cent. of total cases (1736)	99.13	98.27	96.54	93.43

Time from inception of disease bacilli disappeared,	28th day.	21st day.	14th day.	7th day.
Number of cases	1468	1131	558	57
Per cent. of total cases	84.57	65.09	31.91	3.28

Time from inception of disease bacilli disappeared,	6th day.	5th day.	4th day.	3d day.
Number of cases	34	24	14	4
Per cent. of total cases	1.96	1.38	0.81	0.23

In the remaining 15 cases, or 0.87 per cent. of the total, the bacilli were found to have disappeared as follows: On the 57th day, 1; 59th day, 2; 60th day, 1; 62d day, 1; 64th day, 1; 65th day, 2; 68th, 72d, 73d, 74th, 75th, 77th, and 93d days, 1 each.

These figures corroborate the conclusion drawn from observation of cases during the previous year—viz. that in a large proportion of all cases (about four-fifths) the Klebs-Löffler bacillus disappears by the end of the fourth week from the beginning of the disease; that in about two-thirds of all cases it disappears by the end of the third week; and in one-third of all cases by the end of the second week; while in a small proportion of cases (about 3 per cent.) disappearance occurs within one week from the inception of the disease.

The length of time elapsing between the inception of the disease and the date of the last culture showing the presence of the Klebs-Löffler bacillus in the throat of each patient was tabulated for the above 1736 cases, and for 414 additional cases, making a total of 2150 cases. This increased number is due to the fact that for various reasons (death of the patient, etc.) no final culture showing the disappearance of the bacilli was made in the additional cases. As stated for the previous tabulation, the average interval between the last culture showing the presence of the bacilli and that showing their disappearance is probably about eight days, the additional cases in which no final culture was taken, of course, excepted. The bacilli may, therefore, have persisted in many cases for a longer period than that recorded.

Of the 2150 cases tabulated, in 864 the last cultures showing bacilli to be present were made within six days or less from the inception of the disease, and may be considered in the main as made for diagnosis.

The remaining 1286 cases are tabulated as follows:

Time from inception of disease, bacilli present,	7th day and over.	14th day and over.
Number of cases	1286	741
Per cent. of total cases (2150)	59.81	34.46

Time from inception of disease, bacilli present,	21st day and over.	28th day and over.	35th day and over.	42d day and over.
Number of cases	328	155	68	31
Per cent. of total cases	15.25	7.21	3.16	1.44

Time from inception of disease, bacilli present,	49th day and over.	56th day and over.
Number of cases	16	9
Per cent. of total cases	0.79	0.42

In the 9 cases in which cultures showed the presence of the bacilli for 56 days and over from the inception of the disease these cultures were made as follows: One each on the 57th, 58th, 60th, 61st, 62d, 63d, 64th, 88th, 90th, and 91st days, respectively. The above tabulation is chiefly of interest as showing the long persistence of the Klebs-Löffler bacillus in the throat in exceptional cases.

The virulence of the bacilli thus persisting has been tested in a number of cases, with results entirely confirmatory of those reported for the previous year. In every case tested the bacilli retained their virulence irrespective of the duration of persistence in the throat. The case in which the bacilli were found to be present on the 91st day presents points of special interest. It was that of a child three months old when first coming under observation, in which the clinical symptoms were confined to a simple nasal discharge. There were no constitutional symptoms whatever. The nurse, and later the mother of the child, contracted diphtheria from it, the disease in the mother's case being of a severe type. The bacilli were tested at frequent intervals up to five weeks from the inception of the disease, and were found to be virulent in every instance.

The presence of non-virulent diphtheria bacilli in a certain number of healthy throats made it necessary to test the virulence of bacilli from mild sore throats before being able to diagnosticate them as certainly diphtheria bacilli. For practical reasons, however, we are satisfied with establishing extreme probability from the simple microscopical examination of the bacilli.

What are the means by which diphtheria is transmitted?

The facts detailed already throw important light on the manner in which diphtheria is transmitted.

As related to this question, let us first consider very briefly what is known of the duration of life of the Löffler bacillus outside of the body. In actual experiment it has been found to live for long periods of time—namely, by Hofmann, on blood serum for one hundred and fifty-five days; by Löffler and by myself for seven months; and in gelatin, by Klein, for eighteen months. The bacilli have been found to live in bits of dried membrane by Löffler for fourteen weeks, by myself for seventeen, and by Roux and Yersin for twenty weeks. Dried on silk threads, Abel reports they may sometimes live for one hundred and seventy-two days, and upon a child's plaything, which had been kept in a dark place, they lived for five months.

As examples of the manner in which diphtheria may be contracted he gives the following from Johannessen: A teacher developed diphtheria from passing the night in a room in which three weeks before a fatal case had occurred. A child developed diphtheria after putting on the clothing worn by a child which had died of diphtheria two months before. In a number of isolated dwellings diphtheria developed nearly a year after previous outbreaks, without there being any apparent possibility of a new infection taking place from the outside. I have met with a number of cases where the infected bedding or clothing has undoubtedly been the source of the infection.

The Sources of the Virulent Bacilli are—1. From the pseudo-membrane, exudate, or discharges from diphtheria patients. 2. From the secretions of the nose and throat of convalescent cases of diphtheria in which the virulent bacilli persist. 3. From the throats of healthy individuals who acquired the bacilli from being in contact with others having virulent germs on their persons or clothing. In such cases the bacilli may sometimes live and develop for days or weeks in the throat without causing any lesion.

When we consider that it is only the severe types of diphtheria which remain isolated during actual illness, the wonder is, not that so many, but that so few persons contract the disease. This seems to be more remarkable when we observe that in a city like New York the whole tenement-house district, at least, is an infected area. This has become evident from the observations made by the Department.

It has been the practice of the New York Health Department during the last year to plat upon a city map the location and date of every case of diphtheria in which the diagnosis had been settled by bacteriological examination. After several months the map presented a very striking appearance. Wherever the densely crowded tenements were located, there the marks were very numerous, while in the districts occupied by private residences very few cases were indicated as having occurred. It was also apparent that cases were far less abundant, as a rule, where the tenements were in small groups than in the regions of the city where they covered large sections. At the end of six months there were square miles in which nearly every block occupied by tenement-houses contained marks indicating the occurrence of 1 or more cases of diphtheria; and in some blocks many cases (15 to 25) had occurred.

As the platting went on from time to time the map showed the infection of a new area of the city, and often the subsequent appearance of a local epidemic. It was interesting to note two varieties of these local epidemics: in one the subsequent cases evidently were from neighborhood infection, while in the second variety the infection was as evidently derived from schools, since a whole school district would suddenly become the seat of scattered cases. At times, in a certain area of the city from which several schools drew their scholars, all the cases of diphtheria would occur (as investigation showed) in families whose children attended one school, the children of the other schools being for the time exempt.

Another fact noted, perhaps as important as the foregoing, was that with the most careful inquiry it was impossible to find any connection with preceding cases of diphtheria in about one half of the first cases of diphtheria occurring in different houses.

The two following histories are instructive as showing that special conditions, which are largely unknown to us, determine in every individual the occurrence or escape from diphtheria under exposure: Two children in a family were taken sick with diphtheria and removed to the hospital. The servant (who was and remained apparently healthy) went to another family, where the youngest child developed diphtheria a week later. In the mean time a case developed in the family living in the next apartments. There were in this latter family three other children who were not isolated at all from the sick child, yet none of these developed diphtheria.

The child of a man who kept a candy store developed diphtheria; there were four other children in the family, and these were in no way isolated from the sick, yet none of them acquired the disease; but children who bought candy at the store and other children coming in contact with these in school developed it. The secondary cases ceased to develop as soon as the candy store had been closed.

Many similar histories could be given to illustrate the fact that the majority of persons, and even, perhaps, the majority of children, are not ordinarily very susceptible to diphtheria, and that in addition to receiving the germs of the disease into the respiratory passages they must be in a condition favorable to the development of the disease.

It seems to be generally true that the more malignant a case of diphtheria is the more likely it is to cause diphtheria in others. This may be due to the high grade of virulence possessed by the bacilli, or to the peculiar association of other micro-organisms in the membrane, or to the wider dissemination of the infectious matter through the discharges.

It is also well known that young children are much more susceptible to diphtheria than older persons. It is comparatively rare for the parents of children sick with diphtheria to contract the disease, although in nearly every case they must at some time receive the germs into their throats.

The blood of many adults has been shown to have antitoxic properties to the diphtheria poison. At times, however, parents and nurses become infected, as in the following cases:

(*A*) Two months before a child living on the floor below the present case had diphtheria. Until a few days before the sickness of the patient the two families had kept apart. For the last few days they had visited each other, and the first patient, the mother, carried the child who had recovered from diphtheria. When the mother became ill she was still allowed to nurse and carry her children. Three days later her two children were discovered to have contracted the disease. The mother, too sick longer to nurse her children, confided their care to the father, who himself became infected. Antiseptic cleansing of the nostrils and throat was neither used in treatment nor prophylaxis in these cases before their admission to the hospital.

(*B*) In another case, five weeks before, there existed diphtheria in the flat below. The first new patient taken sick was a child, aged two and a half years, three days later another, aged four, and then the mother herself became ill. The children died; the mother went to the hospital and finally recovered. When she left home her seven months' baby went to a friend's, where, three days later, two of the children developed diphtheria, and then finally the baby itself. The baby came to the hospital and died, and one of the other children died.

From the throat the bacilli may be deposited upon the hands, other parts of the person, on handkerchiefs, bed linen, clothes, toys, and eating utensils. Under favorable conditions they may live from one to eight weeks on these infected substances, and under exceptional circumstances, as when the light is excluded and sufficient moisture is present, for eight or nine months. As the infected persons and things are scattered, the bacilli may be carried to healthy persons long distances away from the original disease. As time passes the number of living bacilli diminish, and where they are dry enough to float as dust they soon die.

Conditions Favoring the Growth of the Bacillus and its Length of Life Outside of the Body.—Diphtheria bacilli probably do not increase in water, on walls, carpets, etc., but they may possibly in milk, meat, and soups; but even here the saprophytic bacteria are apt to crowd them out. Low temperature, moist air, and darkness protect the life of the bacilli. In warm weather either the germs quickly dry and die, or if moisture is present other germs grow and displace them. The prolonged light of summer also aids in killing them. Artificial heat in winter may do the same. Sea air is more favorable to the life of the germs than the drier, clearer climates.

Thus in dark, damp cellars and basements we would expect most favorable conditions for the increase of disease. The habit of quickly cleansing dirty clothing prevents the spread of diphtheria, while putting

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From one of the isolated island cottages a mother, a nurse, and two hildren left the island for their home on the mainland at the time of the outbreak, but before its nature was suspected. The nurse com-ained of a sore throat, and when at home developed diphtheria. Being a physician's family, the nurse was carefully isolated. After recovery everything which had been in contact with her was burned or disinfected. Ten days after she returned to the care of the children, and hree days later the eldest child contracted diphtheria and died. Here person who was supposed to have entirely recovered still carried infection.

From another cottage on the island, after diphtheria had broken out, a grandmother with one of the children returned home to New Haven, developed diphtheria, and died. This was the origin of other cases in that city. A young man who was mentioned as coming to the cottages ill on the day of the first cases returned home three days later and died of diphtheria.

It may be stated that although the drainage and sanitary conditions on the island were not at that time first class, yet they were no worse than in many other resorts, and to them could not be attributed the outbreak. In the year following but two cases occurred on Fisher's Island.

THE BACTERIOLOGY OF PSEUDO-DIPHTHERIA.

The pseudo-membranous inflammations which frequently complicate scarlatina (page 594), and to a less extent other infectious diseases, are, as a rule, not diphtheritic in character, and bacteriological examinations will show the diphtheria bacilli to be absent. The same is true for the ordinary acute cases of tonsillitis and pharyngitis and for some of the cases of acute pseudo-membranous laryngitis.

Thus in the exudate in 40 cases of this character which I carefully examined bacteriologically, the cultures from all contained streptococci, and on most of the plates the streptococci far outnumbered all other micro-organisms.

As in normal throats, so here, the streptococci taken from different cases, or even from different colonies of the same case, differed greatly in their growth and appearance. In most of the plates the long chained streptococci resembling the streptococcus pyogenes were the most numerous, but in quite a number the short chained cocci were in the majority. Staphylococci were often present in large numbers, and other bacteria were frequently added.

Communicability.—Persuaded by my clinical experience and by the results of examinations of normal throats, that streptococci were probably harmless while the mucous membranes were intact, I tried the following experiment:

Inoculation of Human Throats with Streptococci.—A very thick culture was made on agar plates from a severe follicular tonsillitis in a young child, so that there was obtained a luxuriant growth of streptococci growing both in long and short chains, and also of other micrococci. A large amount of these mingled bacteria were, with the permission of a patient, plastered on a swab and then rubbed gently on his right tonsil and into its crypts. He felt a peculiar sensation in the tonsil for some twelve hours; this then passed away, and was probably simply the result of the mechanical irritation.

The next morning the tonsil appeared healthy except for a small patch in a crypt; from this and from the throat cultures were made. The plates gave very numerous colonies of streptococci, while cultures made from the same regions the day previous to the experiment gave very few streptococci.

A second trial was made in a similar way from a culture of streptococcus pyogenes, eighteen hours old, from a case of extensive pseudomembrane and tonsillar abscess. The results here were also entirely negative, except for the increase of streptococci in the throat for some days. With this same streptococcus the tonsils of two other adults were daubed, and with similar negative results.

These trials having shown that in three throats the application of streptococci from cultures made from virulent cases of tonsillitis produced no effect, a different experiment was tried. On two separate occasions a sterile swab was rubbed on the tonsils in a case of severe tonsillitis, and then immediately rubbed on a healthy tonsil. In neither case was there any inflammation excited. On the third day after the last experiment a sudden fall in the temperature occurred, and after exposure a follicular tonsillitis developed, such as frequently has followed previous similar exposures.

After rubbing the bacteria on the tonsils patients were cautioned against eating or drinking for some hours, and used no antiseptic gargles for several days. They were also carefully guarded against taking cold.

Though these trials are only a few in number, they are enough to make it seem probable that the pyogenic cocci are not sufficient, as a rule, to excite an inflammation in the throat. A change appears necessary in the mucous membranes, either from the influence of some infectious disease or of some exposure, before the bacteria find the throat a proper soil for rapid increase and the mucous membrane vulnerable to their action.

The following clinical cases confirm these views, and are cases in which the communication of the disease seems at first glance certain:

(1) A family of eight—mother aged forty-five, six children whose ages ranged from twenty-five to ten, and a grandchild, aged two—slept in two rooms of a tenement just under the roof. Two days previously a heavy snow had fallen, and the day before the roof leaked, thus causing the rooms to be very damp. The next morning four of the children had more or less marked tonsillitis, with follicular deposits or croupous patches, and on the following day the baby had an attack of croup.

(2) In a school for young girls, on a day early in the winter, five were taken with follicular tonsillitis, and on the next day three more were attacked.

(3) A nurse attends a patient with croupous tonsillitis, and has to pass frequently from the warm room to a much cooler hallway. On the third day the nurse is attacked with an inflammation much like that of his patient. The physician in charge ascribes it to a direct infection from the patient to the nurse.

In many other similar cases the same exposure to cold, wet, or other

rious influences which caused the first cases is the probable cause
ne later cases, and not a direct infection.

Of very many cases of pseudo-diphtheria examined, only a minority
been in known contact with others having similar inflamma-
. Another important consideration tending to show that exposure
r than direct infection is usually the exciting cause is the fact that
se inflammations are very prevalent in the cold and wet months.
out the first of December they begin to multiply in dispensary and
vate practice, and increase till April; then slowly diminish until
ne, to remain very infrequent until winter approaches. This rapid
ncrease in the late winter and early spring is not found to be true to
e same degree in diphtheria. The histories of many of these cases
ould indicate that the bacteria already present in the throat had been excited to a new growth by some exposure, rather than that a new infection had been received.

Some of these croupous inflammations may indeed be due to a recent direct infection, for one would expect that the bacteria from a fresh inflammation would be somewhat more virulent than those which had long lain dormant in the throat. The proof of this is, however, difficult, for it is impossible to tell from cultures and the histories often give no assistance. Where attendants on the sick or persons in schools and hotels are attacked after other cases have developed, it is difficult to determine whether they have derived the disease directly from the previous patients or have developed it simply because they were subjected to the same sanitary influences as the first. The important fact is that if persons keep themselves from exposure to cold and other deleterious influences they are in little danger of contracting this variety of acute throat inflammation.

In order to test to what degree, if any, pseudo-diphtheria is communicated from one person to another, 450 cases, as nearly consecutive as possible, were investigated, all sources of infection were sought for, and the cases were followed up for two weeks after complete convalescence. In none of these was isolation or disinfection enforced by the Health Department. This is such an important question that the results of the investigation of the first 100 consecutive cases is summarized below in tabular form. As a comparison, a summary is given of 50 consecutive cases of true diphtheria which were taken from the same district and at the same time of the year as the first 50 cases of pseudo-diphtheria:

Summary of Tabulated Cases.

	Table 1 (50 families). Pseudo-diphtheria.	Table 2 (50 families). Pseudo-diphtheria.	Table 3 (50 families). True diphtheria.
Total number of cases	56	57	60
History of contact with other cases	7	7	33
No history of contact	49	50	27
Families in which more than one case developed	5	4[1]	13
Recovered	56	53	46
Died	...	4[2]	17
Cases complicated with scarlet fever	4	6[3]	

[1] Two had scarlet fever.

[2] Three had scarlet fever.

[3] Six others had been in contact with scarlet fever, but never showed any characteristic rash.

We find, therefore, in 113 cases of false or pseudo-diphtheria occurring in 100 families, that 14 occurred at the same time with or shortly after some other case, and that it is possible to assume the disease had been directly communicated to them. In 9 of the 100 families more than 1 case developed. In these, as in the other 350 cases of pseudo-diphtheria investigated, it did not seem that secondary cases were any less liable to occur when the primary case was isolated than when it was not. In this connection one should remember that mild throat inflammations are very frequent, especially in the early spring months, and that it is quite possible, where two cases occurred in a family together or within a short time of each other, that they may have both been due to exposure to some common conditions rather than to direct transmission. The presence of streptococci in nearly all healthy throats in New York City renders this assumption almost a probability. The presence of the same germs in healthy throats as well as in those of patients suffering from pseudo-diphtheria prevents us from deciding the point by bacteriological examinations.

All of the 14 cases, except the 3 who had scarlet fever, were mild, and, indeed, leaving out of consideration the cases which occurred as complications of scarlet fever, there was only 1 death in 113 cases of pseudo-diphtheria, and in this case there was no history of infection or contact with other cases.

PATHOLOGICAL ANATOMY OF DIPHTHERIA.—The most characteristic feature of diphtheria is the formation of an exudate or pseudo-membrane. This usually appears on the mucous membrane of the tonsils, uvula, soft palate, pharynx, and nose. It frequently, however, attacks the larynx and bronchi, either primarily or as an extension from the pharynx. Upon the mucous membrane of the tonsils and adjacent organs the lesions usually first appear as white thin patches of exudate or pseudo-membrane. Later in severe cases the membrane becomes thick, covering a large portion of the mucous membrane, and may have a dirty gray or yellowish tinge.

The tissues underlying and surrounding the pseudo-membrane are more or less intensely hyperæmic and swollen. When the membrane is thick and adherent, it leaves on being torn off a bleeding surface which is quickly covered anew by false membrane. In some of the milder cases the exudate may easily be rubbed off and no bleeding occurs.

The membrane may be made of visible layers, and they may be peeled off one from another. This is especially true of that covering the uvula and soft palate, both of which may be œdematous and enormously swollen. The membrane in the larynx and trachea is of less thickness, and usually is less tough, than that of the pharynx and soft palate.

Although, as a rule, the exudate in the larynx is thin and friable, yet at other times it is thick and fibrous, so that a complete cast of the larynx and trachea may be coughed up or torn off. The swelling of the submucous connective tissue in the region of the ventricles of Morgagni, the false cords, and the aryepiglottic folds may give rise to marked obstruction to the breathing space.

The formation of the pseudo-membrane is due partially to the necrosed epithelium, and partly to the deposition of a coagulable serous ate upon it. This is thrown out gradually, and thus may be formed eral layers.

connective tissue of the mucous membrane is hyperæmic and ated. Sooner or later the epithelium under the pseudo-membrane tly or completely lost, and the underlying tissue is covered instead a network of fibrin which contains more or less partly or com- y degenerated epithelial cells and leucocytes.

his network of fibrin frequently extends down into the submucous es. The fibrinous mass may be composed of a very fine reticulum brin or of a narrow meshed network of tolerably thick bands. It v either contain many leucocytes in the spaces of the network or be tly devoid of cellular elements. The superficial layer of the false nbrane is frequently found early in the disease already broken down to granular detritus and permeated by masses of cocci and diphtheria acilli. The degenerated epithelium usually disappears entirely by solu- on or desquamation, but isolated vestiges may still be met with beneath the membrane when the epithelium has not become necrotic in its whole thickness, and also when the exudation has spread over adjoining portions of mucous membrane where the epithelium has not degenerated. The tissues beneath the pseudo-membrane are always more or less the seat of small-celled infiltration, and frequently also of fibrinous exudate or hemorrhage. The bloodvessels are congested, the lymph channels dilated and filled with fluid rich in fibrin.

If the necrosis in diphtheria restricts itself to the epithelium, healing will take place without the formation of a scar.

The necrosis may, however, extend to the connective tissue, in which case the tissue of the latter, including the vessels, may be entirely destroyed. There may be also in the tonsils and adenoid tissues areas of necrosis. In these cases a depression is left which fills up with granulation or cicatricial tissue.

Heart.—The pathological changes in the heart are among the most important lesions in severe diphtheria. Marked parenchymatous degeneration of the heart fibres up to almost complete fatty metamorphosis may occur. The muscle fibres are degenerated, the nuclei are broken down or have disappeared, and the fibres themselves cease to be continuous. The endothelium of the vessels is swollen and the leucocytes are increased, and hemorrhages may be present between the muscle fibres. These alterations are only marked in the late cases; in those quickest fatal only slight parenchymatous changes are apparent. The valves of the heart may be the seat of fibrinous deposits. In the pericardium there may be collections of serous or more rarely purulent fluid.

Kidneys.—In most severe cases the kidneys are in a state of more or less acute nephritis. The kidneys are usually hyperæmic and enlarged, more rarely anæmic. The capsule is commonly non-adherent; the surface of the kidney is smooth, and is frequently the seat of small hemorrhages. Upon the cut surface the markings are indistinct and show degenerative parenchymatous changes. The cortex is thickened and reddish gray or yellowish gray in color. Microscopically, the signs of marked parenchymatous changes are evident up to complete necrosis of the epithelium lining the tubules. In these tubules evidences of hemorrhages and casts are found. The epithelium of the glomerular capsules is swollen and proliferated, and the vessels of the tufts are compressed by hemorrhages and exudates into the capsule. The endothelium in the walls of the kidney vessels is found proliferated or undergoing degeneration. Frequent and small hemorrhages occur through the walls of the vessels. In severe cases the urine contains abundant albumin, degenerated kidney epithelium, leucocytes, and hyaline casts, and in the most severe coarse and fine granular casts. Blood cells are infrequent.

The adenoid tissue of the spleen, intestines, and lymphatic glands shows the same areas of increased leucocytes and the same necrosis and hyaline degeneration of the tissue cells as are found in the kidneys and other organs.

The submaxillary lymph glands are enlarged, often hemorrhagic, and may even be the seat of suppuration. The lungs in cases dying of laryngeal diphtheria are frequently the seat of areas of broncho-pneumonia or of general bronchitis. Subpleural ecchymosis is frequent, and the lungs exhibit areas of atelectasis or emphysema.

Nervous System.—Paralyses of the muscles of the palate, pharynx, heart, and voluntary muscles are due to degeneration of the peripheral nerves. The degeneration extends the whole length of the affected nerves, including the anterior and posterior roots. This is also true of the phrenic and cranial nerves. Minute hemorrhages are frequently present in the nerves. The spinal cord and brain show no marked lesion.

SYMPTOMS OF PHARYNGEAL DIPHTHERIA.—*Mild Cases.*—Those in which the local lesions are moderate in degree and in which the constitutional symptoms are not serious. These may be divided into two classes. In the first the onset is sudden; the temperature rises to 103° F. in the first twelve hours, and then rapidly falls, so as to reach the normal one to two days later. With the rise of temperature the throat symptoms develop. The mucous membranes appear hyperæmic and congested, and after a few hours more or less extensive patches appear on the swollen tonsils, soft palate, pharynx or uvula. The local symptoms increase for twenty-four hours, and then remain stationary. With the rise in temperature and the local signs of inflammation there are rapid pulse, loss of appetite, and some prostration. At the end of forty-eight hours the constitutional symptoms abate. The temperature is rarely above 101° F. The pulse may still be rather rapid, but is regular and of good force. The local inflammation subsides in from three to seven days, and the patient is fairly well except for a slight anæmia.

In the second class the throat inflammation develops slowly. There is a little pain on swallowing. The glands at the angle of the jaw are usually a little swollen and the throat feels sore. Inspection will show slightly swollen tonsils, with follicular deposits of exudate or small patches of pseudo-membrane. The temperature is not elevated more than one or two degrees or it may be normal. Except for slight loss of appetite, restless sleep, and slight prostration the symptoms are mainly those of a subacute throat inflammation. The exudate may be strongly adherent, so that it can only be removed by force, or it may be loosely attached. The diphtheritic deposit remains from two to seven days, and then recovery is established. A moderate amount of anæmia persists for some weeks. Some cases in either of these two types may, instead of recovering, suddenly begin to extend and develop into the ost severe type. Even in these mild cases slight paralysis may occur to three weeks after apparent recovery.

Severe Cases.—Here, again, two extreme types of invasion are noted. local and constitutional symptoms may slowly develop, or they may me fully developed within the first twenty-four to forty-eight hours, r with or without high temperature. In exceptional cases a chill the first symptom noticed.

The mind is usually clear, although in the worst cases mild delirm or stupor may develop. The mucous membrane of the pharynx tonsils is reddened and swollen. The uvula may be œdematous, ongated, and greatly swollen. Portions or all of the mucous memne of the tonsils, the pharynx, and the soft palate are covered with re or less thick and fibrinous pseudo-membrane of a grayish color. glands of the neck and their adjacent tissues may be slightly or markedly swollen. If the nasal cavities are involved, the breathing and voice are affected. From the nose flows a discharge which may be of an intensely irritant character. The nasal obstruction may be partial, in which case the irrigating fluid passes easily, or it may be total, so that it is only possible to force fluid through the nose under high pressure.

After forty-eight to seventy-two hours the fever, if present, commonly subsides. In favorable cases the pulse becomes less frequent, and remains of fair force and regularity. The appetite improves and the intellect remains clear. After forty-eight hours the local symptoms remain stationary from the third to the fifth day, and then the swelling subsides; the membrane begins to loosen at the edges, and soon peels off, leaving a superficially ulcerated surface, or it may more gradually melt away. The glands of the neck decrease in size, and the patient is convalescent and certain to recover unless dangerous paralysis develops.

In other cases the course of the disease is unfavorable. The temperature may fall nearly to the normal, but the pulse becomes more rapid, feeble, and irregular, or it may in certain toxic cases suddenly for a time become very slow, 40 to 50 to the minute. Before death the heart's action usually becomes more irregular and rapid. Other patients grow apathetic. The urine is apt to be scanty and contain albumin and casts. These cases may suddenly develop uræmic convulsions and die, or may gradually waste away. Some develop a persistent nausea and vomit all food. Others suffer from paralysis of deglutition and of the muscles of respiration. Still others seem to be recovering from the diphtheria when the symptoms and physical signs of pneumonia develop. The temperature then rises to 103° or 104° or even 106° F.

In other cases the false membrane does not limit itself to the pharynx, but spreads to the larynx. These patients then have added the special symptoms due to obstruction to the breathing. Finally, there are a group of cases that seem to die as if from gradual systemic poisoning by toxin. They lose weight, become pale and anæmic, have no appetite, the tongue is dry and coated, and they gradually sink away.

Malignant Cases.—There are certain cases of diphtheria which run an especially malignant course both in children and adults. Within twenty-four hours the tonsils, palate, and lateral portions of the pharynx are covered with thick membrane and are enormously swollen, the breath is sweetish, the saliva dribbles from the mouth, the glands of the neck and their surrounding tissues are greatly swollen. The temperature is frequently but slightly elevated or it may be subnormal. The heart's action is rapid and feeble or it may be very slow and irregular. The intellect, at first clear, becomes cloudy. Within three to five days the most robust die.

Another class of malignant cases are the so-called septic cases. The amount of local swelling and exudate on the tonsils and palate may not be very extensive, but it is of a dirty, gangrenous appearance. If the nostrils are invaded, there is a bad-smelling, thin discharge.

The temperature runs a high, irregular course from 103° to 106° F. The tongue is dry and coated and the appetite is poor. The glands of the neck are moderately or greatly swollen. The extremities are cool, the pulse is rapid and feeble. Pneumonia or suppuration of the middle ear frequently develops. With an irregular high temperature the children become more and more apathetic until death usually supervenes.

SYMPTOMS OF LARYNGEAL DIPHTHERIA.—The symptoms in laryngeal diphtheria differ somewhat according as to whether the process is a primary one or is an extension of a pharyngeal diphtheria to the larynx. In the first case laryngeal symptoms are added to those already present.

In laryngeal diphtheria the symptoms are those due both to the absorption of the poison of diphtheria and to the mechanical obstruction of the larynx. The obstruction occurs more quickly in children than in adults.

The symptoms may develop slowly; the child complains of a sore throat, of a little hoarseness, has loss of appetite and slight fever. There may be a dry, hard cough. In some within twelve to twenty-four hours the hoarseness becomes marked, the breathing is somewhat obstructed, the temperature reaches 100° to 103° F., and the child is restless. Soon, unless relief is given or the process subsides, the symptoms of laryngeal obstruction are fully developed. The respiration is noisy; inspiration and expiration are labored and prolonged. Cyanosis is developed, and there is marked recession of the soft parts of the chest in the epigastric and jugular regions. The accessory muscles of respiration are called into action and the chest is held expanded. In spite of every exertion inspiration and expiration are insufficient.

At short intervals the child will sink back as if exhausted, the breathing is feebler, and for a moment or two the child dozes, only to awaken again to struggle for air. It throws itself about the bed—lies first on one side, then on the other. Until cyanosis is marked the intellect may be clear. Frequent desire to urinate is manifested, which adds to the distress of the child. As the obstruction increases attacks of almost complete suffocation take place; the child struggles violently for air, sitting up and using all its powers. After a time respiration may become freer, and the child sinks back only to have renewed spasms later. Sooner or later it becomes exhausted; the breathing becomes more and more feeble; the extremities are cold and the skin is of cadaveric hue. Death follows from an attack of suffocation or slowly by asthenia. The duration of life in fatal cases is usually from two to seven days when operative relief is not given.

In purely laryngeal cases, when operative relief is not given and death results early, the temperature frequently remains but little elealthough in a few it may reach 103°–104° F. If, on the other the lungs are involved, the temperature is, as a rule, elevated 2° or 104°, or exceptionally 106°, F.

fter intubation or tracheotomy the temperature frequently rises, in ore severe cases, within twelve hours to 102°–104° F. When ive relief is attained the breathing becomes natural, mucus and of membrane are coughed out, and the child sinks back to sleep. portion of the cases the relief is permanent, and the patient gresses uninterruptedly to recovery. In others the symptoms of ruction again appear, while in still others a secondary pneumonia elops to delay convalescence or cause death.

SYMPTOMS OF DIPHTHERIA IN DETAIL.—*General Condition.*—re are a moderate number of cases having very limited patches pseudo-membrane in which no appreciable symptoms of constituonal poisoning show themselves. They are mostly discovered beuse of their association with more marked cases. Even mild cases ow loss of appetite and of the desire for work or play. They become ore or less pale and anæmic. The more grave cases soon exhibit vere constitutional effects. They soon have marked prostration, are restless or apathetic, or both by turns. If they live long enough, they become emaciated. The sleep is uneasy. In septic cases mild delirium or stupor may develop. These cases give the impression of being very dangerously ill.

Temperature.—The cases differ greatly. Many, both mild and severe, begin with a temperature of 102° to 104° F. In the great majority the fever subsides, and even in the most severe uncomplicated cases the temperature is apt to range from 98° to 101° after the first forty-eight hours. Some, severe from the start, have a normal or even subnormal temperature.

A certain proportion of septic cases, and all having a complicating pneumonia, develop a high temperature. Other complications, such as otitis or the development of an abscess, will cause elevation of temperature.

A rise of temperature to 103°–104° F. in a case of laryngeal diphtheria indicates usually a beginning bronchitis or pneumonia.

Nervous System.—In the mild cases, except for a certain amount of apathy, no symptoms are present; in the more severe, there may be also observed the general symptoms of mild delirium, restlessness, and rarely convulsions; also, apathy and stupor in the severest cases.

Circulatory Apparatus.—In mild cases the pulse is frequent, and perhaps slightly irregular. In bad cases it may be very frequent, 120–160, and weak. The force of the heart apex beat is diminished and the sounds indistinct. After the third or fourth day the rapid pulse may suddenly become markedly slowed. From 120 it may fall as low as 45 or 50. It is irregular and varies in force. This is an extremely grave symptom. After twenty-four to forty-eight hours, if the patient lives, the pulse is apt to again become rapid and feeble, and so remain until death.

Digestive System.—In the mildest cases there is little digestive disturbance, but in those of any severity loss of appetite is noted. In the worst toxic cases no food at all may be retained. The bowels are not, as a rule, affected.

The Urine.—In the mildest cases, usually no albumin is found in the urine, but exceptionally, after the third or fourth day, it may appear. In the more severe cases casts, kidney detritus, and large quantities of albumin are usually present. In the worst cases partial or total suppression of urine is apt to occur. These may later develop uræmic symptoms.

Lymph Glands.—The lymphatic glands in the neck are usually somewhat enlarged. In the more septic cases they may become enormously swollen. Suppuration is rather infrequent.

Skin.—A small percentage of cases develop a general erythema, which may resemble scarlet fever or measles. An urticaria may also appear. In severe and septic cases hemorrhages occur in the skin as well as in the mucous membranes.

Joints.—The joints, except in septic cases, are very seldom affected in diphtheria.

COMPLICATIONS OF DIPHTHERIA.—*Pneumonia.*—The most feared complication of laryngeal diphtheria is broncho-pneumonia. In pharyngeal diphtheria it occurs but seldom. It may develop within twenty-four hours or it may not occur till convalescence is established. In these a little fever remains, and the lungs give the signs of a moderate bronchitis. The temperature then slowly or quickly rises and the respirations become more rapid. Physical examination shows beginning broncho-pneumonia, perhaps in one or both lower lobes behind, or, again, in disseminated areas throughout both lungs. In these cases the pneumonia is apt to run a subacute but progressive course. After one to three weeks the child succumbs to exhaustion.

Heart Failure.—From the beginning of the separation of the membrane until well into the fifth week all severe cases are in danger of heart failure. When this symptom is threatening the patient is pale and the pulse is small and irregular. It is usually rapid and weak or very slow and irregular, 40–50. The extremities are cold. The mind remains clear and anxious. The attack may pass off or the pulse may be lost: the patient loses consciousness and death comes gradually. Others, apparently well, suddenly become unconscious, and die almost instantaneously of heart failure.

Paralysis.—This is one of the most characteristic symptoms of diphtheria. Frequently with the final separation of the membrane, but also often after weeks, paralysis develops in the muscles of the soft palate, less frequently in those of deglutition, of the eye, of the respiratory organs, or finally of groups of muscles throughout the body. When the palate is affected speech is nasal and fluids regurgitate into the nostrils. When the muscles of accommodation are affected, the child cannot read and the pupils do not react. When the voluntary muscles in general are affected the patient may be completely helpless. As a rule, complete recovery takes place within from three to eight weeks, but in the worst cases marked atrophy occurs and months elapse before recovery takes place.

RELAPSES.—In a small number of cases, after partial or complete disappearance of the membrane, a slight recurrence results. With the exudate's appearance the temperature may rise and the glands of the neck become swollen. As a rule, the lesions clear up in a few days. The lymphatic glands may remain slightly enlarged for weeks or months.

only cases in which a relapse is serious are the laryngeal ones. A pse may occur as late as the fourth week.

DIAGNOSIS OF DIPHTHERIA.—In deciding whether a doubtful case ne of diphtheria or not it is necessary to take into account whether patient has been exposed to diphtheria, to scarlet fever, or to other ectious diseases.

If in any case exposure to diphtheria is known to have occurred, even lightly suspicious sore throat must be regarded as probably a mild htheria. If, on the other hand, no cases of diphtheria have been own to exist in the neighborhood, even cases of a very suspicious ure would probably not be diphtheria.

In judging from the appearance and symptoms of a case one must irst acknowledge that there are certain mild exudative inflammations of the throat belonging both to diphtheria and pseudo-diphtheria which appear exactly alike, have similar symptoms, and similar duration. It is even possible to examine two cases, knowing that one is surely diphtheria and the other surely is not, and yet be unable to determine which is true diphtheria and which is pseudo-diphtheria. It is not meant to imply that a case is one of true diphtheria simply because the diphtheria bacilli are present, but rather that the doubtful cases not only have the diphtheria bacilli in the exudate, but are capable of giving true characteristic diphtheria to others, or later developing it themselves; and that those in whose throats no diphtheria bacilli exist can under no conditions give true characteristic diphtheria to others or develop it themselves. It is indeed true, as a rule, that cases presenting the appearance of ordinary follicular tonsillitis in adults are not diphtheria. It is also true that now and then a case having this appearance is one of diphtheria, and almost every physician has seen such cases from time to time in households infected with diphtheria. On the other hand, in small children mild diphtheria very frequently occurs with the semblance of ordinary follicular tonsillitis, and in large cities where diphtheria is prevalent all such cases must be regarded as more or less suspicious.

Appearances Characteristic of Diphtheria.—The presence of irregular shaped patches of adherent grayish or yellowish gray pseudo-membrane, especially if they are on some other portions than the tonsils, is, as a rule, diagnostic of diphtheria.

Occasionally in scarlatinal angina or in any severe phlegmonous sore throats patches of exudate may appear on the uvula or borders of the faucial pillars, and still the case may not be one of true diphtheria; these are, however, exceptional. Thick grayish pseudo-membranes which cover large portions of the tonsils, soft palate, and nostrils are almost invariably the lesions of true diphtheria.

The majority of cases of pseudo-membranous laryngitis, whether an exudate is present in the pharynx or not, are cases of true diphtheria. Nearly all cases in which membrane is present in the nose are true diphtheria. Where the membrane is limited to the nose the symptoms are, as a rule, very slight.

Most cases of pseudo-membranes and exudates entirely confined to the tonsils in adults are not diphtheria, although a few cases presenting these symptoms are. Cases presenting the appearances found in scarlet fever, in which a thin grayish membrane lines the borders of the uvula and faucial pillars, are rarely diphtheritic. As a rule, pseudo-membraneous inflammations complicating scarlet fever and other infectious diseases are not diphtheria. But from time to time such cases, if they have been exposed to diphtheria, may be complicated by it.

The Exudate in Diphtheria contrasted with that in Pseudo-diphtheria.—As a rule, the exudate in diphtheria is firmly incorporated with the underlying mucous membrane, and cannot be removed without leaving a bleeding surface, at least until convalescence. The tissues surrounding the exudate are more or less inflamed and swollen. In pseudo-diphtheria the exudate is usually loosely attached, collected in small masses, and easily removable. Exceptions, however, occur in both these diseases, so that in true diphtheria the exudate may be easily removed and in pseudo-diphtheria the exudate may be firmly adherent. It is therefore impossible to make diagnosis certain from the adherence of the exudate to the mucous membrane.

The occurrence of albuminuria with casts may enable a probable diagnosis of diphtheria to be made. This may aid both in a case in which the membrane is in a part removed from observation or in one already convalescent. Some pseudo-membranous inflammations which are not diphtheria give rise to nephritis and albuminuria.

Paralysis following a pseudo-membranous inflammation is an almost positive indication that the case was one of diphtheria.

PROGNOSIS OF DIPHTHERIA.—Diphtheria is one of the most difficult of diseases in which to make prognosis. A case which in the first twenty-four hours seems mild may steadily increase in extent and severity until it ends fatally. A case seemingly convalescent may suddenly develop heart paralysis. Laryngeal diphtheria is especially apt to be complicated by pneumonia.

In the smaller cities epidemics vary greatly in their severity from year to year. In the largest cities, however, there are practically always a number of epidemics going on all the time, and the average severity for the whole city does not vary so much. Age has a very marked influence on mortality.

The special dangers to be feared in diphtheria are the invasion of the larynx, the development of broncho-pneumonia, serious paralysis, especially of the heart and respiratory muscles, sepsis, and nephritis.

The following division of the cases of true diphtheria, based on the extent, character, and location of the pseudo-membrane or exudate, after sufficient time has elapsed for the development of the local lesions, has seemed to me to be of considerable value in prognosis:

(1) Cases in which the pseudo-membranes are very extensive, thick, and firmly incorporated with the underlying swollen mucous membrane. In these the constitutional symptoms are marked, the mortality at all ages is large, and the danger of paralysis great.

(2) Cases in which the development of the pseudo-membranes is largely confined to the larynx and bronchi. This form occurs mostly in young children, is very fatal at all ages, and apt to be complicated by bronchitis or pneumonia.

(3) Cases in which the pseudo-membrane is moderate in amount, involving the tonsils and irregular portions of the uvula and soft palate. These often have marked constitutional and local symptoms

a few days, but nearly always recover except in very young chil-
ı.

Cases in which the pseudo-membrane or exudate is confined to
onsils. These resemble those in the third division, but the
oms are less marked. They all recover unless complications exist.

Cases in which very little or no exudate is ever present, the
us membrane being simply slightly swollen and hyperæmic. These
usually slight symptoms and recover, but are important to diagnose,
ey may infect others.

(6) Cases of pseudo-membranes confined throughout their course to
nose. These occur chiefly in young children. The constitutional
ıptoms are slight, and all so far recorded have recovered. These
s are seldom met with.

(7) Exudates or pseudo-membranes confined to the eyelids, skin,
ectal, and vaginal mucous membranes. The cases confined to the first
vo locations, as a rule, present few constitutional symptoms if the throat
unaffected. When the rectum and vagina are attacked the severity
of the symptoms will depend on the extent of the lesions.

Though the association of streptococci and other bacteria with the Klebs-Löffler bacilli undoubtedly influences the local and general symptoms, yet, as far as can be judged from cultures, they have little influence on the mortality. In the shape and size of the Löffler bacilli I found no constant differences which could be utilized for prognosis.

TREATMENT OF DIPHTHERIA.—*Prophylaxis.*—The patient ill with diphtheria is to be isolated as far as circumstances permit. Wherever possible he should have a separate room. Those who care for the sick should wear a special outer garment. Before leaving the room this gown should be thrown off and the hands carefully washed and rinsed with an antiseptic solution.

The patient should, when old enough, expectorate into some receptacle containing a disinfectant. Everything soiled by the mouth discharges should be disinfected by soaking in some disinfectant solution, by boiling, or by burning. The throat secretions are to be considered dangerous until at least three weeks after the beginning of the attack.

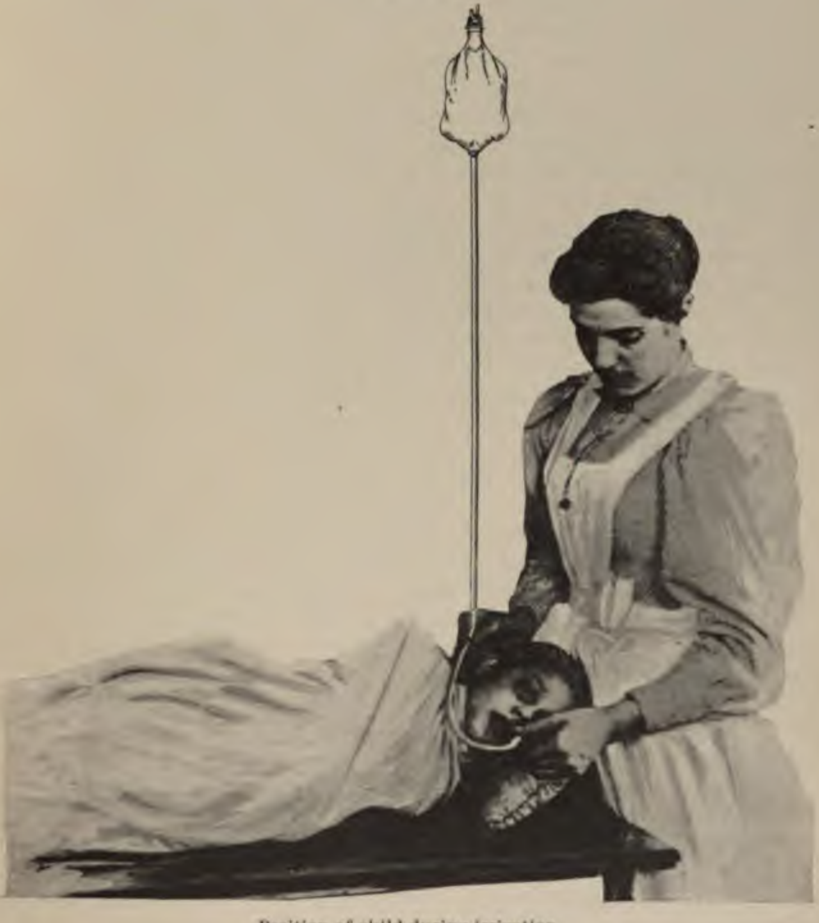
Wherever possible the disappearance of the diphtheria bacilli should be established by the bacteriological examination of cultures. At the conclusion of the illness the bedding and, where possible, the carpets should be disinfected by steam, and the furniture, floor, and walls wiped off with a 1 : 500 solution of bichloride of mercury. Finally, it is well to burn 3 pounds of sulphur to each 1000 cubic feet of air space in the patient's room.

The disposal of the apparently healthy members of an infected family is a matter of great importance. They frequently have already become infected before the first case is diagnosticated, and if sent away they may carry the disease to the children in the families which they visit. It is wise, therefore, not to send them away, unless they have not been exposed to the one taken sick, and only then to places where there are no children. All those who have been exposed or expect to be exposed should receive a moderate injection of antitoxin as a preventive, 100 to 300 units (see page 703) according to age. It is well also to frequently gargle the throat and cleanse the nostrils with some mild cleansing solution, such as Dobell's, or a weak disinfectant, such as 1 : 10,000 aqueous solution of bichloride of mercury. An immunizing dose of antitoxin, together with the frequent cleansing of the throat, will practically ensure an immunity from diphtheria.

Local Treatment.—If one could destroy the diphtheria bacilli at a time when they are localized to one spot of mucous membrane, the disease might be at once aborted and its extension to distant parts might be prevented.

Many clinicians of great experience in the treatment of diphtheria have advised various methods to accomplish this desired result, but personally I believe that their success must always be limited, and for the following reasons: The diphtheria bacilli are not limited to the exact spot where the pseudo-membrane has developed. They are present in the throat secretion, bathing all parts of the pharynx and tonsils

FIG. 49.



Position of child during irrigation.

efore even the local lesions are manifest. Lying thus in the crypts d recesses of the parts, they are not all killed by such antiseptic fluids are attempted to be applied to them. Further, at those places where l lesions are apparent the bacilli are already present beneath the erficial layers of membrane, and cannot be directly influenced by tiseptic fluids.

If the bacteria were upon a dead surface, we could kill them, but to stroy them without injuring the living epithelium is a very different dertaking. Just a year ago a series of experiments were carried out the resident physicians of the New York Hospital for Contagious iseases (Drs. White and Somerset) to test the comparative value of irrigating the nose and throat with simple cleansing solutions and with disinfectants (1 : 4000 bichloride of mercury and 5 to 10 volume solutions of peroxide of hydrogen). After a pretty thorough trial it was very difficult to see more than a trifling advantage in the antiseptic solutions.

If we attempt to kill the bacilli by caustics or actual cautery, we are apt to injure the tissues without killing all of the bacteria, so doing probably more harm than good. I believe, therefore, that we should not use any treatment which will irritate or lacerate the mucous membrane. I believe that no swab should be used to make applications to the mucous membrane unless it is done by the physician or by a trained nurse, and only then with the greatest care. Personally I prefer to trust to irrigation. For the nostrils I prefer a simple tepid salt solution. This is best applied through the fountain syringe. If the nostrils are so firmly plugged that great pressure is needed, then an ordinary hard-rubber syringe can be used. To its point is attached a short rubber tube, ending in a bulb to fit the nostrils. The force needed may be very great, but the shock is of less harm than the continued total occlusion of the nostrils with the probable production of sepsis.

When the local lesions of diphtheria are limited to the tonsils, irrigation of the nostrils is unnecessary, but when the posterior nares are involved, the nostrils should be irrigated three to six times a day. Even weak solutions of peroxide of hydrogen are often very irritating to the nasal mucous membrane. Great care should be taken if it is thought desirable to use this substance in the nostrils. For the irrigation of the mouth and pharynx either a normal salt solution or a 1 : 4000 bichloride of mercury or a five-volume peroxide of hydrogen solution may be employed. If antiseptic solutions are used small blunt-pointed glass or rubber syringes are employed.

In older children and adults the cleansing and soothing effects of irrigation are often marked. In these cases I prefer to use irrigation with warm salt solution every hour or two, and then every three to six hours to irrigate with some antiseptic solution, especially a 1 : 1000 bichloride solution. The irrigation of the throat is, as in the case of the nostrils, best carried out by the fountain syringe. In young children the irrigation of the nose and throat, either with simple salt solution or with antiseptics, every few hours, is of great service unless they struggle against it. Such cases to be handled properly need the greatest amount of good judgment.

When the strength is good and the nostrils and pharynx are full of discharge and membrane, it is well to insist on cleansing by irrigation. When, however, the child is much prostrated, and struggles against it, irrigation may have to be omitted.

The giving internally of the tincture of the chloride of iron or of the bichloride of mercury in small frequent doses has considerable local effect upon the mucous membranes of the throat and pharynx.

In hospital cases the irrigation of the nostrils with salt water, 1 per cent. boric acid solution or 1 : 4000 bichloride solution, has not appeared to cause ear trouble. Indeed, suppuration of the middle ear has been rather less frequent when this method was employed.

General Treatment.—The air in the patient's room should be as pure as possible and kept at a temperature of 70°–72° F.

The treatment of diphtheria by antitoxin will be considered later (page 692).

The drugs suggested for the treatment of diphtheria have been numberless, but few of them have proved themselves as of use generally. At the New York Hospital for Contagious Diseases mild cases are given an abundance of light diet, milk, broth, eggs, etc., and a dose of 1000 units of antitoxin. This and the local treatment is all they receive. More severe cases are given brandy from half an ounce to twelve ounces in the twenty-four hours, according to the severity of the disease and the amount of prostration and the weakness of the heart action. In these severe cases and in any where paralysis threatens, strychnine is given three times a day in doses of $\frac{1}{30}$ to $\frac{1}{100}$ grain. As the patients begin to convalesce they are given the carbonate or albuminate of iron as a tonic if they show much anæmia.

A complicating pneumonia is treated as it is when present in other conditions.

The antipyretics are to be avoided, because of their depressant effect, and also because the temperature is, as a rule, not seriously high in diphtheria.

The tincture of the chloride of iron in moderate doses may be of benefit, both locally and for its tonic effect, though if it causes nausea or vomiting it should be stopped. Large doses do not appear to have any more beneficial effect than small, and are more apt to cause irritation of the stomach. The internal administration of bichloride of mercury has not seemed to me to be of any great value. Good observers advocate small doses of quinine. I myself have had but little experience with its use.

Whenever paralysis of the muscles of deglutition has become sufficiently marked to prevent the swallowing of food, it is necessary to feed through a soft-rubber tube passed through the nose to the pharynx and œsophagus.

TREATMENT OF LARYNGEAL DIPHTHERIA.—For the relief of obstruction in laryngeal diphtheria there is the inhalation of the fumes of subliming calomel, the inhalation of warm steam with or without lime or other additions, the application of warmth or cold over the larynx, and the use of medicines internally, especially those causing nausea or vomiting.

The first two are the most important means of combating the beginning laryngeal obstruction.

Calomel Fumigation.—This was first advocated by Corbin in 1881, has since been extensively used. The inhalation of subliming mel does not, as some claim, destroy the diphtheria bacilli, but it apparently, in some cases, greatly relieve the obstruction with its mpanying symptoms. This so often follows each employment of it there seems no doubt of its action. It does not, however, afford ef in all cases, even when used very early.

The method of employing calomel fumigation varies with the apparatus at hand. The child should be put in an improvised tent so as to nfine the fumes sufficiently to fill the tent with a rather dense white moke. Ten to twenty grains can be thrown on a few live coals placed n a shovel and held under the tent while it sublimes, or a lump of live al may be put in an iron or earthenware vessel and over it a strip of iron or an iron spoon upon which the calomel is placed. In the larger cities a suitable apparatus can be bought ready for use, which is, of course, more convenient.

Steam.—The inhalation of warm steam is certainly at times of great benefit. To the water may be added equal parts of lime water, or to each pint one or two teaspoonfuls of compound tincture of benzoin. The warm damp vapor is the chief thing. The steam should be inhaled as warm as possible, and the patient is protected from the dampness by a covering of oil, muslin, or a thin blanket.

If in a strong child the laryngeal symptoms increase so that it seems as if intubation will soon become necessary, it is well to try the effect of vomiting. For this purpose a dose of ½ to 1 fluidounce of syrup of ipecac should be given every ten minutes until effective. Instead of ipecac, tartar emetic or the yellow subsulphate of mercury, ij–v gr. to a child of two years, and repeated, may be given. If an attack of vomiting does not give appreciable relief, it is not well to repeat it, as it exhausts the child and offers but slight hope of benefit. If a child is much prostrated, it is unwise to resort to emetics at all.

Intubation and Tracheotomy.—If in spite of treatment the laryngeal stenosis advances so far that actual obstruction to breathing is marked and increasing, we must resort to intubation or tracheotomy.

By one or the other of these means we overcome the obstruction to the entrance of air through the larynx, and thus prevent suffocation, unless the membrane is too extensive below the end of the tube. We also aid the expulsion of mucus and portions of membrane through the opening formed by the tube. The insertion of the tube does not, of course, limit the extension of the disease or prevent complications. The apparent improvement due to the removal of the obstacle to respiration will therefore only be permanent when the disease itself is not too severe.

The time at which intubation should be performed is a question of the greatest importance.

The insertion of a tube into the larynx is not wholly a matter of indifference even in trained hands. More or less abrasion of the swollen and inflamed laryngeal mucous membrane may be caused by its insertion, and its presence for several days is very likely to cause a superficial ulceration, either where its lower end impinges on the trachea or where its sides cause pressure.

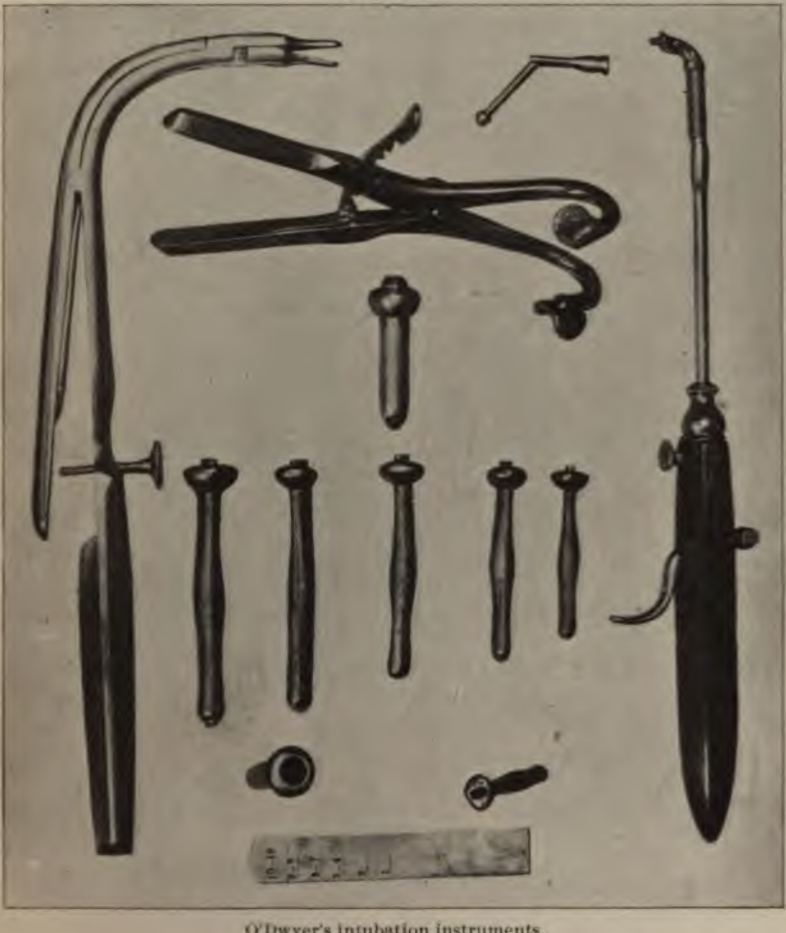
On the other hand, so soon as the laryngeal stenosis becomes so marked that the person struggles for air, and in spite of the struggle sufficient aëration of the blood does not take place, that condition is a great detriment to the condition of the child long before any actual suffocation is impending.

In spite, then, of the possible injury to the larynx of the insertion and retention of the tube, we should not wait too long and thus allow a greater injury to occur.

If, therefore, the stenosis steadily increases and the retraction of the epigastric and jugular regions becomes decided, and cyanosis is evident, it is better not to wait longer.

If it is expected to intubate, one would operate at a somewhat earlier period than if it is intended to do tracheotomy, since the latter is a somewhat more serious procedure.

Fig. 50.



O'Dwyer's intubation instruments.

Intubation Instruments.—The outfit used is that devised by O'Dwyer.

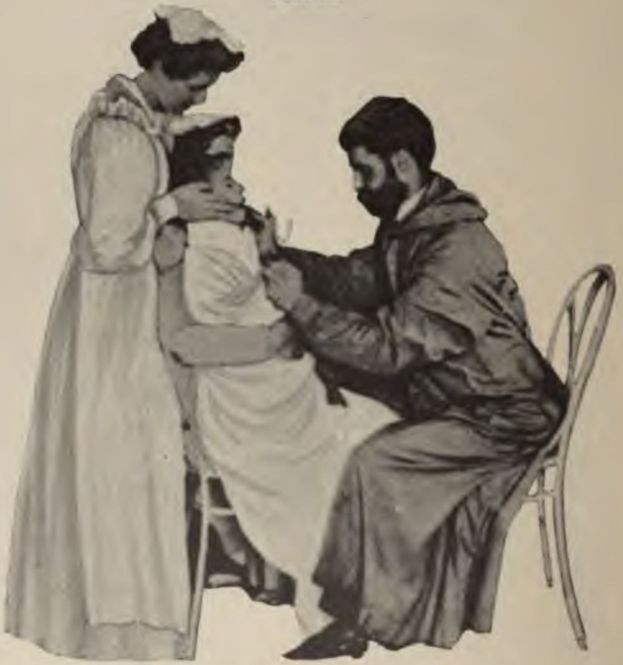
It consists of a series of six tubes of varying sizes, both as to the calibre and length. They are arranged to fit the larynx at different ages; the tubes usually supplied are those suitable for children, but especially prepared tubes for adults can also be procured.

Besides the set of tubes there is an introducer, an extractor, and a mouth gag. The tube as seen in the photograph is enlarged at its upper end posteriorly; there is also a moderate swelling in the middle portion, which fits into the ventricles of the larynx. Through the lip of the upper end of the tube there is a perforation for the passage of a strong thread.

The introducer consists of a straight wooden handle ending in a steel rod, which at its last inch is curved downward at an angle of 90°. It ends in a small screw tip on to which the small rod which holds the tube screws. Over the rod of the instrument a flexible outer tube is attached; this may be shoved down over the rod, thus pushing the tube from the holder after it has been placed in the larynx.

The extractor is shaped like a pair of laryngeal forceps; the lower arm ends in a wooden handle. Through the juncture of the steel and wooden parts there passes a screw which is so placed that it can be made to project a greater or lesser distance from the handle, and thus prevent the full approximation of the two arms of the extractor. This regulates the extent to which the tips can be separated. If by any means, therefore, the tips of the extractor have not entered the tube, they are thus

FIG. 51.



Position of child during operation of intubation.

prevented from spreading too widely apart and injuring the tissues of the larynx.

Intubation in Laryngeal Diphtheria.—Position for Intubation.—The child should be wrapped in a sheet or in a blanket, so as to confine the extremities, but leave the neck exposed. Pin the sheet behind. The child should be held in the lap of one nurse, sitting in upright position with the head against the left shoulder. The mouth gag is inserted in the left side of the mouth, and held in place by a second nurse who stands behind and who at the same time steadies the child's head. The head should be kept erect.

If necessary the child can be intubated lying down, and some, indeed, prefer this position.

Insertion of the Tube.—The index finger of the left hand is passed along the dorsum of the tongue until it feels the epiglottis. It is then passed behind the epiglottis until it touches the arytenoids. In a small child the epiglottis is often difficult to feel, and in any case where there is much swelling it may be impossible to make out its exact location.

To insert the tube, which has been selected of the proper size and placed on the introducer, it is passed along the inner side of the index finger down to the tip of the finger; the handle bars are then raised and the tube is passed downward and forward into the larynx. In doing this the finger is pushed slightly aside by the tube. The beginner is very apt not to pass the tip of the tube sufficiently forward, and may thus pass it into the œsophagus. The tube having passed into the larynx, place the tip of the index finger of the left hand on its upper end, push the tube off with the obturator, and withdraw it.

In the insertion of the tube and in the extraction of the holder one should be sure to keep the tube in the median line. It is also very essential to have the child's head kept perfectly still.

A thread which has been passed through the eye of the head of the tube is left until one is perfectly satisfied that the tube is not clogged with membrane and that it is giving proper relief to the child.

It is also necessary to be sure that the tube has not passed into the pharynx and œsophagus.

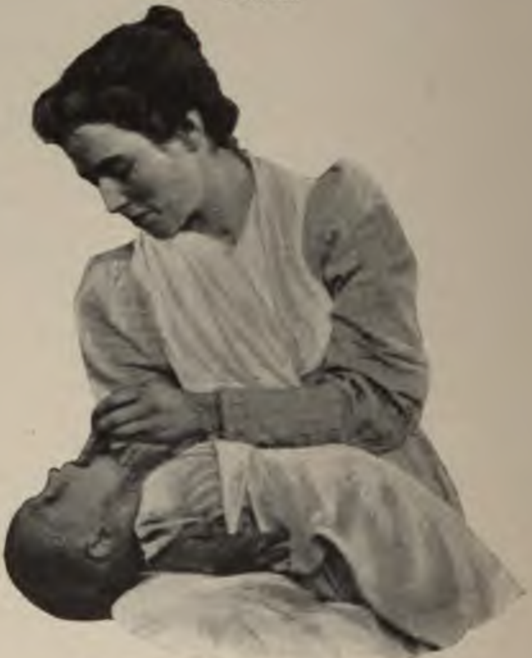
After the insertion of the tube it is well to give the child a little water and whiskey, in order to cause it to cough by the slight irritation; it is also valuable as a stimulant to the child after the exertion occasioned by the passage of the tube.

After the insertion of the tube the operator is usually able to ascertain whether it has relieved the stenosis within a few minutes, but in exceptional cases, where the child is very weak, it may be impossible to determine this for half an hour. In very young children it is possible to intubate without using the gag, but in older children one runs the risk of being severely bitten without it.

Treatment of the Patient while Intubated.—It is frequently the custom to raise slightly the foot of the bed on which the child lies, and it is always well to keep the child prostrate if possible.

A matter of vital importance is the feeding of the child. This is first attempted with the child lying down, with the head depressed below the rest of the body. If the child does not take fluid nourishment in this way, it is allowed to drink in the natural manner. If it is impossible to feed the child by either of these means, it must be fed by a stomach tube passed through the nose into the stomach. For a child of one to two years the tube should be the size of a No. 6 catheter; for a child of three to four years, a No. 8 catheter. Some physicians prefer, instead of a fluid diet, food which is of greater consistency or even entirely solid At the Willard Parker Hospital for Contagious Diseases, however, fluid diet is, as a rule, preferred.

FIG. 52.



Feeding child wearing intubation tube.

Extraction of the Tube.—At any time after the insertion of the tube it may be coughed up, or it may become obstructed by membrane either blocking the tube or filling up the trachea below. Whenever the tube becomes obstructed it must be instantly removed. In those cases in which, however, the tube is neither coughed up nor obstructed it is found best to leave it in for such a period that seven days have elapsed from the time of the beginning stenosis. If the tube is removed earlier, it will usually have to be replaced, with the danger always of creating slight abrasions or injuries of the larynx.

Method of Extracting the Tube.—The child is held in exactly the same position as for intubation. As in intubation the index finger of the left hand is passed along the dorsum of the tongue, then behind the epiglottis, and downward until it feels the end of the tube and makes out its lumen. The finger should detect whether the tube is lying in the proper position—that is, with the long diameter of the opening lying from before downward. The extractor is then passed along the finger, as the tube was in intubation, until one brings the tip of the extractor against the side of the tip of the finger and the opening into the head of the tube. A beginner must be careful that he does not mistake the shoulder of the extractor for the tube. The handle of the extractor should be raised to a horizontal position, as otherwise only the tip will enter into the tube and the danger of slipping will be very great. The extraction is accomplished by lifting the extractor with its tube until it touches the hard palate, and then the handle is lowered through an arc of 90° and the tube removed. In young children, as in intubation, a gag is not necessary. The extractor, as stated in the description of the instrument on page 688, is provided with a safeguard in the shape of a screw which passes through the lower arm of the handle so as to come in contact with the upper arm. This, by proper adjustment, serves a double purpose. First, it prevents the opening of the jaws of the extractor to such a degree as to injure the soft parts if by chance it should not have entered the lumen of the tube; and, second, it gives information as to whether the tip of the extractor is within the lumen of the tube. For with the screw properly set it will be impossible to obtain the click of one arm of the extractor against the screw if the tips are within the lumen of the tube. When, for any reason, a person is unskilled in the extraction of the tube—and for the beginner the extraction is rather more difficult than the insertion—it is possible in an emergency, in the majority of cases, to easily expel the tube by placing the child face downward with the body slightly elevated, and pressing gently against the trachea along its anterior surface, just below the end of the intubation tube. This method should not be used when one is skilled in removing the tube with the extractor, because there is always danger of causing abrasions of the mucous membranes by too forcible pressure. The tube is removed from the mouth by the finger.

Another form of extractor has been used, that devised by Dillon Brown. This is employed like the previous method when one is not skilled in handling the extractor invented by O'Dwyer. In order to use the Brown extractor a special set of intubation tubes is necessary. These have, at the anterior edge of the head, a small loop. This allows an extractor to be used which is attached to the finger and which ends in a little hook. The finger is passed, with the hook attached, over the dorsum of the tongue until it touches the tube, when the hook is passed into the loop and the tube thus removed. In cases where a great deal of swelling is present the swollen tissues are apt to cover up the little loop on the end of the tube and make it very difficult to remove the tube by this extractor.

At the hospital, immediately after the extraction of the tube, the child is given $\frac{1}{64}$ grain of morphine hypodermically, and an ice bag is applied to the larynx. It is sought in this way to lessen the irritation and swelling in the larynx. The child is still kept in a recumbent position for one or two days.

When the tube does not give relief, one of two things is possible
either a tube with a much larger lumen, but which is lighter and sho
may be inserted, or tracheotomy must be performed.
will one of these large calibre tubes succeed where th
failed. Tracheotomy will more often give relief, b

is so extensive that in spite of the temporary improvement the ority of the cases finally succumb.

though at the autopsy frequently a moderate degree of ulceration nd, yet it is probable that this takes place chiefly in those cases re the resistance of the tissues has been greatly lessened by the severe c infection.

There are a few cases where, on account of paralysis or the growth of nulations, the child is unable to breathe without the tube. Here a ondary tracheotomy may be tried, and the granulations may be removed by operation. The tube probably predisposes somewhat to pneumonia, and in some cases it seriously interferes with the feeding of the ld. In those cases where the ordinary tube does not afford sufficient ace for the expectoration of the mucus and loosening membrane, the ider tube devised by O'Dwyer may be substituted. These are usually oad cases.

The Advantages and Disadvantages of Intubation and Tracheotomy Compared.—Intubation has the following advantages: It requires no cutting operation and causes no danger of hemorrhage or of external wound infection. The consent of the parents is more easily obtained. It is generally easily performed by one accustomed to the procedure. It requires but one, or preferably two, assistants. The time of leaving the tube in the throat averages less. The nursing is simpler.

The objections are: the danger of the ulceration of the tissues from pressure, the difficulty of administering nutriment, and the more frequent insufficiency of the relief afforded. In about 2 per cent. of the cases it will be found that the child cannot breathe without the tube for weeks after the disappearance of all other symptoms. If this is due to paralysis, recovery usually takes place after weeks or months. If the obstruction is due to a growth of granulations, it may be necessary to remove them by operation, and to do this a preliminary tracheotomy will generally be necessary.

Commonly in America intubation is first performed in all cases, and tracheotomy only in those in which the relief is not satisfactory, either at the time of the insertion of the tube or later. Here tracheotomy may give free breathing, but in a majority of these cases the membrane, still extending, will again produce obstruction, and thus the fatal termination is only somewhat delayed.

Diphtheria Antitoxin in the Treatment of Diphtheria and as an Immunizing Agent.—The foundation for the treatment of diphtheria, and to a less extent of certain other diseases, with antitoxin rests upon the fact—and it is well to keep in view that it is a fact—that the blood and serum of animals immunized against certain diseases contain substances, called antitoxins, which, when injected into healthy animals, will give them immunity to the same diseases. Further, not only will the serum confer immunity to later infection, but will, if not given too late, prevent the otherwise fatal outcome of the disease in animals already ill. The result is much the same whether the antitoxin is given to an animal before or at the same time as the dose of toxin or virulent bacteria, but varies greatly for each hour's delay in giving the antitoxin after the infection has taken place. The longer this period is the greater the amount of antitoxin needed and the more doubtful the recovery.

The first publication demonstrating the antitoxic power of the serum of animals immunized against diphtheria in the treatment of experimental diphtheria was made by von Behring in December, 1890.

The first trial of antitoxin serum in human diphtheria was made in the autumn of 1891 in the city of Berlin.

Mode of Action of Antitoxin.—It seems probable that antitoxin does not act directly in any way upon the toxin, but rather upon the tissue elements in such a way as to make them insusceptible to the poisonous action of the toxin.

After the cells have been to a certain extent affected by the toxin, the protective power of the antitoxin can no longer be exerted and the lesions progress in spite of it.

Derivation of Antitoxin.—From the fact that the antitoxin developed in the blood of an animal is only antitoxic for the special toxin with which it was injected—that is, tetanus antitoxin only immunizes against tetanus poison, diphtheria antitoxin against diphtheria poison, etc.—it would appear that the antitoxin must be derived from the toxin. A substance which seems to be the same as diphtheria antitoxin has indeed been obtained from diphtheria toxin by electrolysis.

There are certain facts, however, which teach us that the living tissue elements probably are actively associated in the transformation. Thus in animals freshly immunized small doses of toxin will produce far larger amounts of antitoxin than these same doses will produce when the animals have been long under treatment. The amount of antitoxin produced seems to depend more on the extent of the reaction of the animal to the injections than on the amounts of toxin introduced. The diphtheria antitoxin is obtained for medicinal purposes almost entirely from horses. These animals receive repeated doses of diphtheria poison in constantly increasing amounts until, after from two to four months, their blood serum contains sufficient amounts of antitoxin to be serviceable for treatment in human diphtheria.

The power of the diphtheria antitoxin to neutralize the poisonous effects of the diphtheria toxin in animals is, as before said, an absolute fact which has been shown to be uniformly true in thousands of experiments. We have every reason to expect that, since the toxin in human diphtheria is, so far as we can determine, exactly the same toxin as that in diphtheria in animals, this power of the antitoxin to make harmless the toxin will manifest itself in man under similar conditions.

We have every reason, therefore, to expect it to almost certainly prevent, for a time at least, an attack of diphtheria, but as to its exact value at different stages in the development of the disease only clinical experience can determine.

"If," as Welch[1] so well states it, "the curative effects of the serum are brought about through the agency of the living cells of the body, we can understand why these effects will not follow the injection of the serum with the certainty and precision of a chemical reaction. The cells must be in a condition to respond in a proper way to the introduction of the antitoxic serum. For one reason or another this responsive power may be in abeyance; we know that it may be weakened or destroyed by the intense or prolonged action of diphtheria poisons, or by other previous and coexistent diseases, or by inherent weakness, or there may even be some individual idiosyncrasy which hinders the customary response of the cells to the antitoxin.

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[1] Welch, *Bulletin of the Johns Hopkins Hospital*, July, 1895.

"Clinical experience shows that cases of diphtheria inherently refractory to antitoxic serum are exceptional, although they do certainly from time to time occur."

The antitoxic serum exerts no bactericidal effect upon the diphtheria bacillus, although when administered in proper quantities sufficiently early in the disease it arrests the spread of the local inflammation which is caused by the bacillus. Virulent bacilli, so far as the results in New York go, seem to persist in the throat for about as long a period as in the cases formerly not treated with antitoxin.

One of the most important characters of antitoxin is that it requires a definite quantity to neutralize the effects of a definite quantity of toxin. In animals the curative dose of antitoxin stands in a definite quantitative relation to the size and susceptibility of the individual and to the amount and intensity of the poison in the system. If an animal does not receive a sufficient amount of antitoxin, it frequently dies almost as quickly as one having received no antitoxin at all. We have no method of determining how much and how virulent the poison may be in a given case of human diphtheria, nor how susceptible to toxin the patient may be. The dose of antitoxin, therefore, in human diphtheria is empirical, the main factors to determine it being the age of the patient, the estimated duration of the disease up to the time of the administration of the remedy, and, most important of all, the severity and extent of the disease.

As the serum is capable of inducing unpleasant symptoms, it is desirable not to give an excessive quantity. It is, however, necessary not to err on the opposite side and give too little, for it is far more important to give sufficient to overcome the dangers than to endeavor to avoid by too small a dose the after possible unpleasant effects.

It is very important to bear in mind that the diphtheria antitoxin only immunizes against the poison of the diphtheria bacilli, and that, in so far as the lesions in any case of diphtheria are due to the action of the poisons produced by other bacteria, these lesions will be in no way influenced.

The lesions of diphtheria are, as a rule, at the beginning mainly due to the action of the toxin of the diphtheria bacillus, but later inflammation may take place, due to other bacteria, so that septicæmia or pneumonia may develop, which, being due not so much to the diphtheria bacilli as to streptococci or pneumococci, will of course advance without regard to the use of the diphtheria antitoxin.

These facts impress us still further with the importance of using the antitoxin early, for we are not only thus enabled to immunize the cells against diphtheria toxin, but by preventing the advance of the disease we ward off these later infections.

We have no way of gauging accurately at any given period of the disease the extent of the damage already inflicted upon the cells of the body. If the nerve cells have already been so damaged that paralysis must follow, or the cardiac nerve cells or muscular fibres have been similarly injured, or the renal epithelium so affected that degeneration and nephritis ensue, the administration of antitoxin cannot restore those cells which are already on the way to degeneration and death.

The effects which follow the injection of the antitoxic serum in individual cases are not new and strange. Nothing happens which the physician may not have occasionally seen to happen in cases treated in the ordinary way. In severe as well as in slight cases of diphtheria he may have seen an apparently progressive local process quickly arrested and the general symptoms promptly abated.

But, as Welch puts it, why should anything new and strange happen after the administration of antitoxin? Cure by antitoxin is, if our theories are correct, by nature's own remedial agent. That which is new and strange is the frequency with which, in case after case, the early injection of antitoxin promptly arrests the local inflammation and checks the constitutional disturbances.

Recovery following treatment by antitoxin is of such a natural kind that in any favorable case a physician may repeatedly feel that the whole process might have resulted without the use of the remedy. One can therefore understand why it should be, as a rule, those with the advantage of a large experience in the treatment of diphtheria by antitoxin who are most decided in expressing their opinion as to its beneficial effects.

Antitoxic Serum.—The serum should be clear and free from any bacterial growth. Each cubic centimetre should contain at least 100 units. When possible, serum of five times that strength of antitoxin should be used. An antitoxin normal unit is ten times the amount of serum required to protect a guinea-pig weighing 250 grammes from death when ten times the fatal dose of toxin is mixed with the serum and the mixture injected subcutaneously into the animal. As measured by Roux's method, 50 antitoxin normal units are equivalent to about 1 cc. of serum having a protective power of 1 to 50,000. The contents of von Behring's vial No. 1 are therefore about equal to 12 cc. of a serum 1 to 50,000. The contents of von Behring's vial No. 2 about equals 10 cc. of a serum 1 to 100,000, or 20 cc. of a serum 1 to 50,000. The serum manufactured in this country is usually put up in vials of from 5 to 10 cc., each cubic centimetre having from 100 to 500 antitoxin units.

Dose.—The size of the dose should be measured chiefly by the extent and intensity of the disease; also, but to a less degree, by the size of the patient and the duration of the illness. For young children with but moderate lesions of the tonsils or palate a single dose of 1000 to 1500 units will suffice. For older children and adults 1000 to 2000 units should be given. In children who are already seriously ill or who already show the toxic effects, or in whom the larynx is involved, a dose of 1500 to 3000 units, 10–14 cc. No. 3 or 3 cc. No. 7, is necessary.

If the symptoms do not abate, another 1000 to 2000 units may be given on the following day. In a few cases still a third injection is required. Exceptionally a week or ten days after administering the antitoxin a slight return of exudate may appear; here another moderate injection is indicated. Where these doses have not benefited it is doubtful if larger ones will succeed.

At the New York Hospital for Contagious Diseases for several ns one half of the severe cases received on admission 3000 units, gain on the following day 3000 more. If no improvement fol- l, a third 3000 units were given. The other half received 2000 on admission, and a second 2000 in eighteen hours. So far as one judge, those receiving the lesser amount did as well as those ing the very large amounts. On the other hand, no additional eeable effects were noticed from the larger quantities.

munization.—When children or adults have been much exposed phtheria they may be protected by the administration of from 100 00 antitoxin normal units (5 to 15 minims or $\frac{1}{3}$ to 1 cc. of a high e antitoxin). The protection lasts from three to eight weeks. The edy is administered by deep hypodermic injection from an ordinary podermic syringe.

Some point on the anterior surface of the body should be chosen for e injection where there is an abundance of subcutaneous cellular tissue, ch as the anterior surface or side of the thorax or the outer surface of he thigh. Before the remedy is administered the skin should be carefully washed with some disinfecting solution.

The syringe should be sterile. The solution is rapidly absorbed, and it is better not to employ massage over the point of injection.

Results Obtained by Antitoxin Treatment.—The value of antitoxin in diphtheria is, in my opinion, established, yet the treatment is so recent that it seems to me wise to give certain reliable statistics, so that readers may themselves to a certain extent have a basis for forming their own opinions. I shall select for this purpose figures from two hospitals: first, from the Willard Parker Hospital for Contagious Diseases of New York City, where all cases of diphtheria occurring in the city and needing hospital treatment are sent. I select this hospital because I have watched nearly all the cases personally and am familiar with the results before the use of antitoxin. For the second hospital I have selected the Kaiser-und-Kaiserin Friedrich Augusta Hospital of Berlin, because Baginsky[1] has reported these cases in such a thorough manner, and because the figures show what one can hope to accomplish under favorable conditions. First I will give a statistical summary of the results obtained in the treatment of diphtheria with antitoxin at the Willard Parker Hospital during the year 1895 as contrasted with the previous year:

Mortality in Willard Parker Hospital in 1895 and First Quarter of 1896, when Antitoxin was Employed in all Cases, and in 1894, when it was Employed in but few.

All cases, even moribund, included.	Cases.	Deaths.	Percentage.
1894	606	208	34.32
1895	716	189	26.39
1896 (first quarter)	180	41	22.77

It is necessary to state that the cases were admitted under exactly the same conditions during 1895 as in previous years. As seen in this table, in the fourth quarter of 1894, the time just preceding the use of antitoxin, the mortality was high. Indeed, during the month of December all of the 12 intubated cases died. There is no reason to suppose that the epidemic was of a milder character when the use of the antitoxin was begun. There were indeed through the winter months an unusual number of laryngeal cases.

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[1] *The Serum Therapy in Diphtheria,* Adolph Baginsky, Berlin, 1895.

Deaths according to Day of Disease upon which Treatment was Begun.

	Antitoxin, 1895.		No antitoxin, 1894.	
Day upon which treatment was begun.	Cases.	Mortality, percentage.	Cases.	Mortality, percentage.
First day	113	8.85	57	19.29
Second day	146	24.32	131	35.11
Third day	132	24.27	131	32.82
Fourth day	102	30.39	88	37.50
Fifth day and over	221	34.36	199	87.69
Total	714	28.39	606	34.32

Careful investigation at the homes of many of the patients showed that they had been sick, as a rule, longer than stated in the hospitals records. This table is nevertheless of great value. It shows, in the first place, so far as figures can show, that the epidemics of 1895 and 1894 were of about the same severity, the cases admitted after the beginning of the fifth day having about the same mortality in both years. The cases admitted, however, on the first two days show a very different mortality. This is true also, but to a less marked extent, for the cases in which treatment was begun on the third day. Too much emphasis cannot be placed upon the importance of giving antitoxin early in diphtheria. There is no doubt in my mind that most cases which die in spite of the early administration of the usual treatment would be saved if antitoxin were given within the first thirty-six hours of visible disease.

Let us now turn attention to the statistics reported by Baginsky. They certainly give a very favorable showing for antitoxin.

Baginsky[1] reports the following as the results of the treatment of diphtheria before and after the use of antitoxin:

	Cases receiving no antitoxin, 1890–1894.			Cases receiving antitoxin, 1894–1895.		
Year.	Cases.	Deaths.	Percentage.	Cases.	Deaths.	Percentage.
0–2	243	154	63.36	87	22	25.28
2–4	333	176	52.85	146	25	17.12
4–6	274	104	37.98	116	20	17.24
6–8	197	54	27.41	79	9	11.39
8–10	124	24	19.35	58	3	5.17
10–12	73	11	15.07	20	2	10.00
12–14	43	6	13.95	15	2	13.30

Laryngeal Diphtheria under Antitoxin Treatment (Baginsky).

	Cases.	Deaths.	Percentage mortality.
Intubated	25	5	20
Tracheotomized	11	8	72
	36	13	30½
Not intubated	11	0	0
Total laryngeal cases	47	13	23

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[1] *Loc. cit.*

A most convincing demonstration of the power of antitoxin is rnished by the experience of Baginsky during an involuntary pause the serum treatment caused by failure in the supply of serum. ween March 15, 1894, and March 15, 1895, there were treated in nsky's service by antitoxin 525 children, with a fatality of 15.6 cent. During the period of forced interruption of the serum treatnt, this period being chiefly the months of August and September, 6 children were treated without antitoxin, with a fatality of 48.4 r cent. There was absolutely no selection of cases in either group. his comments upon this experience Baginsky says: "It is all the more emarkable as the ratio of mortality of those treated with the serum oth before and after the period of interruption varied within very nall percentage figures.

"If one will permit figures to speak at all, there has scarcely been made on human beings a more demonstrative test of the curative power of a therapeutic agent. It was an experiment forced upon us, but it proved to us how terrible was the form of disease which we were treating, and how numerous would have been the victims without the use of the healing serum."

Another proof that the cause of the lower death rate is not due to the cases being milder is seen in the universal lowering of the death rate in laryngeal diphtheria. I quote again a paragraph from Welch's summary: "No one can claim that laryngeal diphtheria requiring intubation or tracheotomy is anything but a severe disease.

"If the benefits of antitoxin are unmistakably manifested in these operated cases of croup, then the test is an *experimentum crucis*, and puts an end to the objection of those who assert that the apparently favorable results of serum therapy in diphtheria are attributable mainly to the large proportion of mild cases treated.

"Before the introduction of the serum treatment a collective investigation was set on foot by the German Gesellschaft für Kinderheilkunde to determine the average fatality following intubation.

"In 1893 von Ranke reported to the society that 1445 cases of diphtheria with laryngeal stenosis treated by intubation gave a fatality of 62.5 per cent. This result was interpreted in favor of intubation as opposed to tracheotomy. There is a difference of 33.6 per cent. between this percentage and that obtained from our 342 intubation cases treated with antitoxin. This difference is so great that, after making all possible allowance for differences in the series of cases entering into the two groups of statistics, it seems impossible to explain it otherwise than as a powerful additional support of the arguments already presented in favor of the claims of antitoxin. Here certainly the objection that the cases treated by antitoxin were light ones cannot be made.

"During the enforced two months' (August and September) interruption of the serum treatment in Baginsky's service there were 116 cases of laryngo-stenosis, with a fatality of 62.2 per cent., as opposed to a fatality of 37.8 per cent. in the serum periods which preceded and followed the pause. The percentage of operations rose to 55.2 as opposed to 18.1 per cent. during the periods of serum treatment, and this without any change in the general character of the cases admitted.

"During the serum periods there were more intubations than tracheotomies, whereas during the pause there were 45 tracheotomies and 19 intubations, 13 of the latter requiring secondary tracheotomy."

The following statistics, showing the results of treatment with antitoxin in 24,768 cases, as contrasted with those not receiving antitoxin, have been furnished me by Dr. Girade. They have been compiled without the least attempt to favor antitoxin. They comprise all the cases given in the journals by observers reporting over 10 cases:

TABLE I. *Mortality in Diphtheria treated with Antitoxin and Previous Mortality without Antitoxin.*

	Cases.	Deaths.	Mortality, per cent.	Previous mortality, per cent.
Hospital cases	15,560	3009	19.0	
Private cases	9,208	995	10.1	
Total	24,768	4004	16.0	30 to 40

(Cases moribund at the time or dying within twenty-four hours after are included in these statistics.)

TABLE II. *Mortality of Diphtheria treated With and Without Antitoxin at the Same Time or during the Same Period.*

	Cases.	Deaths.	Mortality, per cent.
Hospital with antitoxin	7986	1754	21.0
" without antitoxin	9039	3309	36.4
Private with antitoxin	3161	412	13.0
" without antitoxin	4255	1717	40.0
Total with antitoxin	11,147	2161	19.1
" without antitoxin	13,294	5026	37.8

(The antitoxin cases were often severe cases taken as tests.)

TABLE III. *Mortality of Operative and Nonoperative Cases of Diphtheria treated with Antitoxin, and Previous Mortality of Operative Cases without Antitoxin.*

	Cases.	Deaths.	Mortality, per cent.	Previous mortality, per cent.
Nonoperative cases	12,066	1491	13.5	
Operative cases	3,082	1135	36.7	65
Total	15,148	2626	16.6	
Tracheotomy	1355	569	42.0	70
Intubation	1173	361	30.8	51.5
Intubation and second tracheotomy	52	37	71.0	
Intubation or tracheotomy.	502	168	33.2	

TABLE IV. *Mortality of Diphtheria with Antitoxin, arranged according to Age.*

	Cases.	Deaths.	Mortality, per cent.
0–2 years	1494	469	31.4
2–5 years	3678	762	20.7
5–10 years	3184	473	14.8
Over 10 years	1444	99	6.9
Total	9800	1803	18.4 (chiefly hospital).

TABLE V. *Mortality of Diphtheria with Antitoxin, arranged according to Day of Disease on which Treatment was Commenced.*

	Cases.	Deaths.	Mortality, per cent.
First and second day	4,232	267	6.3
Third and fourth day	3,870	656	17.2
After fourth day	1,984	605	34.6
Day unknown	339	44	13.0
Total	10,425	1672	16.0

(Cases moribund or dying within twenty-four hours included.)

Leaving statistics, let us look more closely at the results noticed in individual cases.

Beneficial Results of Antitoxin.—Upon the Local Process.—In the cases in which I have made or seen an injection made within the first twenty-four hours of the disease the results have been so remarkable that I have attributed them to the antitoxin. Following are the histories of two typical cases:

CASE I. A boy eleven years old had had for twelve hours malaise, with pain on swallowing. Inspection showed the tonsils and portions of the palate to be covered with a soft, slightly adherent exudate. The boy was injected with 1000 units, and twelve hours later his throat was clear and temperature normal. I do not believe this would have been a severe case without antitoxin, but the effect seemed magical.

CASE II. The second case was a baby one year old, with a slight croupy cough for twenty-four hours, and stenosis just beginning. Temperature 102; patient restless and without desire for food. Injected 600 units, and found the baby on the following morning practically well.

When the disease has progressed several days—and these cases are the ones seen in the hospital—the benefit is not so apparent. I believe, however, that a marked effect is still produced. There have been very few cases, indeed, of pharyngeal or tonsillar diphtheria in which the membrane has increased after admission. I believe that the same result has taken place in laryngeal diphtheria. Even in well developed cases the pseudo-membrane itself has seemed to me to separate somewhat more quickly than formerly, there being usually seen after thirty-six to forty-eight hours a line of demarkation separating the membrane and making it look like a slough ready to be cast off. The swelling of the throat tissues and of the glands of the neck also appears to me to begin to abate earlier. The ulcerated surface left in some cases after the separation of the membrane is covered with a soft exudate until healing occurs some days later. In laryngeal diphtheria, if the intubation could be put off for eighteen hours, it was, with very few exceptions, avoided altogether. The time during which the cases remained intubated seemed to me to be shorter than before the use of antitoxin. Many children coughed up their tubes in from twenty-four to forty-eight hours, and quite a number were able to do without them afterward. Others required the tube from three to eight days. Exceptional cases occurred, as previous to the use of antitoxin, when the tube had to be worn for weeks. The general condition of patients was beneficially influenced. The loss of appetite and the apathetic condition are less apt to occur, and when present seem more quickly relieved. In cases in which treatment was begun very late, as a rule no good effects were noted.

Ill Effects of Antitoxin Serum.—A small percentage of the cases have a slight rise of temperature immediately after an injection. In a very few cases abscesses develop at the seat of the injection. This is a preventable accident.

Rashes.—These are peculiar to the serum injections. They are undoubtedly partly due to the horse serum, not altogether to the antitoxin. They occur in from 5 to 20 per cent. of the cases according to the characteristics of the serum. The eruption may be limited to the point of injection, or may more or less completely cover the whole body. It most often appears as an urticaria, but may very closely resemble scarlet fever or more rarely measles. It usually develops between the tenth and fifteenth days. In some cases all the forms may be united in one person. Following the eruption, desquamation may occur. In about one fifth of the cases there is a rise in temperature of 2°–4° F. This lasts from one to three days. In a small percentage of cases there is accompanying the rash great tenderness over the joints of the extremities. These pains last, as a rule, one to four days. In one case in the hospital the joint affection was more serious. The child, aged fifteen months, was admitted on April 25th with severe stenosis. The temperature was 101° F. The child was intubated and did well. It received two injections of 1200 units each. On the 27th there was a macular eruption over the body; twenty-four hours later the joints of the hands and feet became intensely painful. The child dreaded the least handling. The knees and the two joints of the left thumb became more swollen, and appeared like acute articular rheumatism. Before the eruption developed the child's condition was rendered more serious by the appearance of a broncho-pneumonia, which continued gradually to increase until death, two weeks later. There have been, in New York, four cases reported in which the joint lesions persisted for several weeks. These all finally recovered. The urticaria and erythema which at times accompany the rise in temperature are in certain cases very distressing, and in a person already prostrated might not be wholly without danger to the patient.

I have seen in watching over 1500 cases no serious effects upon the heart, kidney, or nervous system which I attribute to antitoxin, with the possible exception of two cases of scarlatina complicated with diphtheria. In these two there was an almost complete suppression of the urine. This was probably due to the scarlet fever and diphtheria, and not to the antitoxin.

Since it has been suggested by some that injections of antitoxin with the accompanying horse serum have a disintegrating effect upon the red cells of the blood, we investigated the matter very carefully in the laboratory of the New York Health Department.

J. S. Billings, Jr., one of the assistant bacteriologists of the department, examined very carefully the blood in 15 babies after they had received doses of antitoxin for immunization. The children received from 200 to 400 units each. No alteration was discovered in character of the red or white blood cells. The number of the white cells practically remained unchanged. The number of the red cells sh
however, in half of the cases, a very interesting change: i

15 a gradual diminution in their number took place from day to r until by the sixth day there was a loss of from 200,000 to 600,000 each 5,000,000 of their cells. After this date the number rapidly reased, until upon the fourteenth day the numbers had returned to normal. In adults receiving 1200 units the same result took e. From 6,000,000 the count dropped to 5,400,000, and then rerned to the normal at the end of ten days. None of these persons wed any evidences of anaemia except in the examination of the blood. e cells contained their normal amount of haemoglobin. The blood a series of cases of diphtheria treated with antitoxin was compared ith that in a number in which no antitoxin was used. The diminution the number of the red blood cells was greater in those not receiving e antitoxin. No marked effect was noticed upon the number of the hite cells.

Limitations of Antitoxin.—Diphtheria antitoxin, so far as is known, as no action upon the cells in causing them to resist any poisons other than those produced by the diphtheria bacilli. Here we see at once a limitation in the cure of the complex disease called diphtheria, for it is as correct to class some of the cases met with as pneumonia complicated with diphtheria as to call them diphtheria complicated with pneumonia. Upon the pneumonia, so far as it is not due to the diphtheria bacillus, one cannot hope that the antitoxin will have any curative effect. Another limitation is suggested by the results of experiments upon animals. It is known that after the infection has proceeded to a moderate degree it cannot be arrested by antitoxin. Experience shows that in human beings also the cells no longer react to antitoxin after a certain degree of poisoning has taken place, and this point in some cases seems to occur very early. I doubt if we are justified in saying that in these the actual lesions have progressed so far that without any further poisoning life has become impossible. I believe it may be possible that even after the administration of antitoxin the poison goes on producing further lesions, the cells already affected by the toxin not responding to the antitoxin. There are exceptional cases in which even when the antitoxin is given early it apparently fails to fortify the cells against the diphtheria poison.

In the hospital the effects of antitoxin upon laryngeal diphtheria, though in one way striking, are in another disappointing. More children live than formerly, but it seems as though still more should live. Many survive the acute infection only to die later of the complicating bronchopneumonia. It has occurred in cases of diphtheria treated with antitoxin, just as in cases not so treated, that a relapse may take place four or five weeks after recovery from the disease. Pneumonia is much less frequent in private practice, and seems to be less frequent under hospital treatment abroad. Special hospital conditions were probably accountable for it.

The following case illustrates a class which end fatally, and yet, although the disease is thoroughly established and the patients are under the influence of the toxin, one cannot help feeling disappointment when, although they respond to the antitoxin partially, they finally die.

Case III. Alice M——, aged sixteen years, a girl strong and well nourished, was admitted to the hospital on the third day of her illness; the glands of her neck, both tonsils, and the peritonsillar tissues were greatly swollen. The whole area extending back into the pharynx was covered by a thick dirty white adherent membrane; her nostrils were partially obstructed; temperature 99° F.; pulse 108. Her intellect was clear. 1000 units of antitoxin were injected; same amount was injected twenty-four hours later. Thirty hours after her admission the swelling and infiltration were much less; the membrane had lessened and was of more benign character. Her heart was irregular, but she felt better; the temperature was 99° F. and the pulse 110. Four days after her admission her heart action became much more irregular, and her pulse was but 66, falling the next day to 34. The patient had repeated attacks of heart failure; all nourishment was vomited, so that stimulants had to be given by rectum. The patient died on the fifth day of her stay in the hospital. Autopsy showed extreme fatty degeneration of the heart and extensive degeneration of the other organs.

Use of Diphtheria Antitoxin in Preventing by Immunization the Development of Diphtheria.—The results obtained under my observation in a number of children's asylums and hospitals and in the crowded tenements of New York have been so very favorable that they encourage the hope that a general use of antitoxin for immunization will to a large extent limit the spread of diphtheria. At the Mt. Vernon branch of the New York Infant Asylum a case of diphtheria developed on February 18, 1894. Cases continued to develop from time to time, so that in September alone 14 cases occurred. From that time until January 14th there was hardly a day in which a case did not develop. On January 16th and 17th, 221 children were each injected with from 100 to 200 units of von Behring's serum. No bad effects were seen, and during the next month but 1 case of diphtheria developed; this was on the fourteenth day. From February 22d to 27th, 5 cases appeared, and the children were again immunized. This time they each received from 125 to 225 units of von Behring's standard of a serum prepared under the direction of the New York City Health Department.

No cases appeared after the second immunization for a period of five weeks. Cultures made from the throats of those in the neighborhood of this case showed diphtheria bacilli in the throats of 6 of the children. These 6 were given 200 units each on March 30th. One of these children developed a small patch two weeks later, but had no constitutional symptoms. A case developed on May 3d, and one on May 27th, in the children immunized on February 27th. The hospital has remained since then free of diphtheria, so that no third general immunization has been thought necessary.

At the Nursery and Child's Hospital in New York in the three weeks preceding April 18, 1895, there were 15 cases of diphtheria. Upon that day 136 children, varying in age from three weeks to four years, were immunized by receiving from 50 to 200 units each. The children showed no bad effects from the injections. A temporary rise in temperature occurred in one fourth of them, which lasted for six to twelve hours. From the day of the injections to the present time no diphtheria has developed in the hospital, with two very interesting exceptions—a physician and a nurse who had not been immunized. Since then the hospital has been free from diphtheria.

At the House of Reception of the New York Catholic Protectory 2 cases of diphtheria developed on July 7, and 3 cases on July 8th and 9th, 1895. On July 9th and 10th the remaining 67 children were injected with 150 to 600 units each. (The children's ages varied between two and a half and fifteen years.) No diphtheria developed after the injections in any of these children. In August a new set of children were received, and August 5th a case of diphtheria developed among these, and on August 10th a second. On this day the 37 children who comprised the new lot were injected with from 200 to 600 units of the Health Department's serum. No more diphtheria developed.

The dosage was graded as follows:

2 years	1 case	200 units.
3 "	1 "	250 "
6 "	1 "	350 "
7 to 12 years	20 cases	400 to 500 units.
13 to 20 "	14 "	500 to 600 "

The injection having been made in the forenoon, most of the children showed temperatures of from 99° to 99.5° F. the same evening, two or three reaching 100°, and one 100.6° F. During the two days on which observations were made most of the temperatures subsided to normal, a few remaining at 99° F. No cases except those mentioned later showed any constitutional symptoms after the injections. In only 2 cases was there any local irritation. In 1 of these the symptoms promptly subsided without treatment; the other, unfortunately, developed an abscess.

In the last group of cases, 37 in number, specimens of urine were obtained before the injections to compare with those taken after the administration of the serum. The results of the examinations are as follows:

	Before immunization, August 9th.		After immunization, Aug. 11th.		Aug. 13th.
	Sp. gr.	Albumin.	Sp. gr.	Albumin.	Albumin.
Case 1	10.22	Trace.	. .	Negative.	Negative.
" 2	. .	Negative.	10.30	Trace.	"
" 3	. .	"	. .	"	"
" 4	. .	"	. .	"	"
" 5	10.24	30 per cent. in vol.	. .	60 per cent.	"
" 6	. .	Negative.	. .	16 per cent.	"

One child showed 30 per cent. in volume of albumin (the urine, after boiling and the addition of nitric acid, was allowed to stand for twenty-four hours, and the deposit was then estimated) in the urine before treatment, and after the injection there was about 60 per cent. in volume. The urine from the sister of this child showed no albumin before the injection, and gave not the slightest evidence of illness other than the albuminuria at any time, and neither showed any temperature reaction. In both of these cases, as in all the others, the albumin had entirely disappeared two days later.

Nine days after the injections 1 case developed an urticaria which lasted for twenty-four hours. No other cases showing the skin rashes were observed. At the Reception House of the Juvenile Asylum in

New York 4 cases of diphtheria developed during the week ending April 11, 1895. On the 12th the children (to the number of about 70) were injected with from 200 to 400 units.

No cases occurred afterward, except that the boys' attendant and an engineer who handled the clothes from the diphtheria children, and who had received immunizing injections, developed diphtheria.

To me these results seem conclusive as to the immunizing power of injections of from 100 units of antitoxin upward.

Although in these institutions it was impossible to say that any special child would develop diphtheria, still it was an absolute certainty that in each of these institutions more cases would have developed unless in some way the children could be immunized.

About one sixth of the children had slight albuminuria, and a much smaller percentage developed it to a greater extent. In none, however, were there any other symptoms pointing to any deleterious action on the kidneys, and in none was the albuminuria more than transitory.

In the blood there was noticed, as before stated, a slight temporary diminution in the number of the red blood cells; no other changes were observed.

Immunization by New York Health Department Inspectors in Infected Families.—For some months past in families in which diphtheria has occurred, and in which there were other children exposed to infection, the Health Department inspectors, acting on their own judgment as to the necessity, have immunized some of these exposed persons. Most of these cases have been among the tenement-house population. A few cases taken at random from the reports of the inspectors illustrate the method:

Family 1.—Five children in family; 2 cases of diphtheria; the other 3 children, aged nine, eleven, and thirteen years, were immunized; no further cases occurred.

Family 2.—Three children in family; 1 case of diphtheria; 2 other children, aged eight and sixteen years, immunized; 1 child had diphtheria bacilli in the throat at the time. No further cases of diphtheria

Family 3.—Three children in family; 1 case of diphtheria, 1 of the remaining 2 children immunized; second child, aged sixteen, not immunized. This child developed diphtheria three weeks later, and was successfully treated with the antitoxin.

Cases like the foregoing might be repeated almost indefinitely. 232 persons had been immunized in this way up to October 1, 1895, and of these at least 93 (many of the others were not examined bacteriologically before being immunized) had diphtheria bacilli present in their throats when treated. The cases were kept under observation until the premises had been disinfected, and this was done until the throats of all were free from bacilli.

Among the 232 persons immunized by the inspectors 3 developed membranous croup within twenty-four hours of the time when they were treated, who in fact had diphtheria before being injected, but all recovered. Three others had mild pharyngeal diphtheria—developing 1 on the nineteenth, 1 on the thirtieth, and 1 on the thirty-first day after injection, and 1 developed a fatal diphtheria on the fifty-fifth day.

The cases detailed number altogether 1043; 224 of these were imized once with von Behring's serum, and the second time with the ; York Health Department serum. In a large percentage of the le number diphtheria bacilli were present in the throat when the m was administered, and all had been exposed to diphtheria under itions more or less favorable for the transmission of the disease. ng those immunized 3 cases of diphtheria occurred between one . thirty days after the treatment; *i. e.* 1 on the twelfth, 1 on the enteenth, and 1 on the nineteenth day, respectively.

Twelve cases developed diphtheria later as follows: On the thirtieth , 2; thirty-first day, 1; thirty-third day, 1; thirty-seventh day, 1; ty-ninth day, 1; fortieth day, 2; forty-second day, 1; fifty-second y, 1; fifty-fifth day, 1; sixty-sixth day, 1; ninetieth day, 1. The 4 cases that developed croup within twenty-four hours of the injection undoubtedly had the disease at the time of injection.

Table showing the Number of Cases Immunized in New York City, and the Results.

	No. of cases immunized.	No. of units of antitoxin administered.	No. of cases of diphtheria developing among those immunized between 1 and 30 days.	No. of cases of diphtheria developing within 24 hours.	No. of cases of diphtheria developing after 30 days.	No. of cases of diphtheria that occurred in the institutions previous to immunization.
New York Infant Asylum (1st immunization).	224	100 to 200	1 mild on the 19th day.	0	6	107 cases in 108 days.
New York Infant Asylum (2d immunization).	245	125 to 225	1 mild on the 12th day.	0	4	6 cases in 12 days.
Nursery and Child's Hospital	136	50 to 200	0	0	0	46 cases in 90 days; 15 cases in 15 days.
New York Juvenile Asylum	81	150 to 250	0	0	0	12 cases; 3 cases in 2 days.
New York Catholic Protectory	114	150 to 600	0	1	0	5 cases in 3 days.
Bellevue Hospital	11	175 to 225	0	0	0	2 cases in 10 days.
Health Department Inspectors	232	150 to 250	1 mild on the 19th day.	3	3 1 : 30 1 : 31 1 : 55	One or more cases in more than 90 families.
Total	1043	. .	3	4	13	

Altogether, therefore, excluding these, 16 cases of diphtheria occurred among 1014 persons—3 in from one to thirty days, and 13 in from thirty to one hundred and ten days after immunization. These cases were all mild, excepting 2, 1 of which proved fatal from diphtheria, and in the other death seemed to be due to broncho-pneumonia complicated by a mild diphtheria. During ninety days preceding immunization, under practically the same conditions, it may be said that more than 225 cases of diphtheria occurred. By the use of antitoxin it has been possible to stamp out completely diphtheria in four great institutions for the care of children in which it was prevailing in more or less epidemic form. In no instance have there been, so far as can be determined, any serious results from the administration of the remedy for this purpose. The duration of immunity in many cases is apparently not more than thirty days, but it may be for a much longer time. The doses required to confer immunity are probably between 50 and 300 antitoxin units, according to the age of the individual treated.

A summary of cases reported in the journals is as follows:

Immunization by Antitoxin.

Total cases immunized	16,576.
Antitoxin units injected	50 to 1000 (usually 150-200).
Attacked within 30 days	129 mild, all recovered.
Attacked after 30 days	20 mild, all recovered.

(No serious after-effects observed which could be ascribed to the antitoxin injected.)

CONCLUSION ON DIPHTHERIA ANTITOXIN.—Diphtheria antitoxin has a marked curative effect in diphtheria. The results are very striking when the injections are used early in the disease, and when the diphtheria is uncomplicated with pneumonia or sepsis. In well developed cases and in those having complications its benefit is less marked. In cases already profoundly under the influence of the diphtheria toxin and in a dying condition it is useless.

The total amount required in the treatment of a case varies from 1000 to 6000 units of von Behring's standard, and is determined by the severity and duration of the disease and the weight of the patient. An injection of 100 to 300 units of antitoxin in a person will give an almost certain immunity from diphtheria for four weeks. If security is desired for a longer period, the injection must be repeated.

Diphtheria antitoxin will not cure all cases of diphtheria in which the element of mixed infection is marked, even if given early in the disease. It does not destroy the diphtheria bacilli. It is desirable with the antitoxin to use other treatment, both local and constitutional. The injection of diphtheria antitoxin with its accompanying horse serum is attended in a moderate percentage of the cases with disagreeable results, but in very few if any with serious ones. No cases have been observed in which the kidneys showed any evidence of being seriously affected. It does not appear to have any deleterious effects on the blood, other than to cause a moderate temporary diminution in the number of red blood cells, and even this is more than counterbalanced by its lessening the action of the diphtheria poison.

Large injections in persons not having diphtheria are more apt to cause unpleasant and even somewhat serious after-effects, than in those affected by the disease. It is well, therefore, to be fairly sure of the diagnosis in adults, in whom, as a rule, but little danger exists, before giving a full injection.

PSEUDO-DIPHTHERIA, INCLUDING NON-DIPHTHERITIC MEMBRANOUS LARYNGITIS, OR CROUP.

Pseudo-diphtheria is not a distinct disease like diphtheria. The name is used to cover all inflammations of the upper air passages not due to the diphtheria bacilli which simulate the less characteristic cases of diphtheria. The bacteriology of pseudo-diphtheria has been already considered in the earlier part of this article. (See page 670.) Many of the varieties of pseudo-diphtheria are considered under other headings, such as tonsillitis, the throat lesions complicating scarlet fever, acute laryngitis, etc. These will be, however, grouped together here, and briefly considered in connection with a few illustrative cases.

CLINICAL DIVISIONS.—1. Extensive pseudo-membranes, mostly confined to tonsils, soft palate, and pharynx: *a*, uncomplicated; *b*, complicating infectious diseases. 2. Pseudo-membranes involving the larynx. 3. Pseudo-membranes and exudates confined to the tonsils.

1. *Illustrative Cases.—Extensive Pseudo-membranes, confined Chiefly to the Tonsils, Soft Palate, and Pharynx.*—CASE I. Feb. 5th. Female aged eight. Clinical history: Tonsils covered by large, irregular, adherent, whitish patches. Fauces and tonsils swollen and livid in color. Temperature, 104° F.; pulse, 40; respiration, 20.

February 6th. Tonsils, sides and tip of uvula, and faucial pillars covered by a thin, friable, grayish pseudo-membrane, which leaves a bleeding surface on removal. The appearance is as if on a mucous membrane denuded of its superficial epithelium a thick paint had been applied.

February 7th. Tonsils and faucial pillars clear of membrane; superficial ulceration on pillars, and adherent membrane to uvula. Temperature remains between 102° and 104° F.; pulse, 118 to 130; respiration, 24 to 30.

February 16th. Ulceration on uvula nearly healed. Temperature normal. No albumin in urine at any time. No great prostration.

CASE II. February 27th. Female, aged nineteen. Clinical history: Both tonsils and adjacent surfaces of uvula covered by a thin gray membrane. Tonsils much swollen and painful. Great hyperæmia of pharynx. Temperature, 99.6° F.; pulse, 100. No albumin in urine.

February 29th. All symptoms abated. Membrane disappeared. No swelling of glands.

CASE III. February 3d. Female, aged sixteen months. Clinical history: Thin, adherent, semi-translucent membrane on tonsils and adjacent surfaces of uvula. Nostrils occluded, but no membrane visible. Croupy voice and breathing. Slight swelling of glands of neck. Temperature, 100.2° F.; pulse, 136; respiration, 34.

February 4th. Membrane nearly disappeared. Child nearly well.

February 6th. Throat perfectly clean. Child is well. Evening temperature, 100° F.; pulse, 118; respiration, 28.

CASE IV. February 3d. Jennie K——, aged eighteen. Clinical history: Thin adherent pseudo-membrane on sides and tip of uvula. Some hyperæmia of pharynx. Temperature, 101.4° F.; pulse, 100. Membrane remained four days. After the first day temperature and pulse sank to the normal, and patient did not appear sick. No albumin in urine. Discharged on the sixth day.

In these cases there is first a redness and swelling of the mucous membrane of the pharynx, tonsils, and fauces, with later a thin purulent discharge. Cultures at this time reveal very abundant colonies of streptococci. The epithelium of the inflamed mucous membrane, where the irritation is intensified by the contact and friction of adjacent surfaces, becomes necrotic, and the denuded surface becomes covered by a thin pseudo-membrane, composed mostly of streptococci held together by a small amount of fibrin. The streptococci may also penetrate into the denuded mucous membrane.

If one looks at a well marked case, having the patient open the mouth slightly, and depresses the tongue just a little, the inflamed uvula is seen lying between and against the swollen tonsils. On the portions of the uvula thus irritated by contact, on the faucial pillars lying against the tonsils, and, in extreme cases, on the lateral walls of the pharynx and on the soft palate spreading up from the sides of the uvula, one finds the pseudo-membrane, which is always light grayish in color, thin, and friable. On removal a bleeding surface is disclosed. When astringent applications are not used the membrane usually disappears gradually, and does not scale off in firm pieces of considerable size, as in many cases of true diphtheria.

In none of these cases is there apt to be a fatal result, nor great prostration, after-emaciation, or paralysis. Except that these cases were not complicated by suppuration of the cervical glands and diffuse cellulitis, they otherwise appear to be the same as the pseudo-membranous inflammations complicating scarlet fever, the greater severity in the latter being probably due to the influence of the scarlet fever poison. The temperature curve varies greatly in different cases. The bacteriological diagnosis is of great value in prognosis.

Pseudo-membranous Inflammations complicating Scarlatina.—Confined chiefly to tonsils, soft palate, and pharynx. Except for complications these give exactly the same clinical appearances as those not complicating infectious diseases.

The complicating pseudo-membranous inflammation occurring early adds greatly to the severity of the case; thus in 10 cases of scarlet fever observed by me, in which a severe complicating croupous inflammation appeared early, 6 died. Of the 7 in which it appeared late, all recovered. Of the 6 fatal cases, 2 had extensive gangrenous cellulitis, beginning in the neck, spreading over the chest, and causing the sloughing of an extensive portion of skin. A third had diffuse suppuration in and about the cervical glands.

2. *Pseudo-membranes Involving the Larynx caused by Streptococci.*—CASE I. February 13th. Female, aged five. Recovered. Clinical history: On admission to the hospital cyanotic from laryngeal obstruction; intubated, relieved; very slight, adherent, thin, pearl-gray patches on uvula. Temperature, 100° F.; pulse, 102; respiration, 22.

February 17th. Patient never seemed sick; exudation on uvula disappeared; no albumin in urine; tube remained in five days.

CASE II. March 18th. Female, aged one. Recovered. Clinical history: Very small white patch, slightly adherent to right tonsil; laryngeal dyspnœa; made to vomit, and fumigated with calomel, but without relief; intubated five hours after arrival in hospital. Temperature, 99.6° F.; pulse, 120; respiration, 30.

March 20th. Seems about well; tube still retained; some albumin in urine.

March 26th. Tube removed; temperature never above 100° F.

Bacterial examination: Cultures gave abundant colonies of the long-chained streptococcus.

CASE III. March 19th. Male, aged four. Died. Clinical history: Intubated before admission to hospital. Temperature, 100° F.; pulse, 130; respiration, 32. No membrane visible in throat; some white, flaky membrane coughed up; large amount of albumin in urine.

March 22d. Chest full of râles; child drowsy and cyanotic, although there is no laryngeal obstruction. Temperature, 102° F.; pulse, 150; respiration, 42. Swallows with difficulty. Died on 23d.

CASE IV. March 21st. Female, aged four. Clinical history: Marked laryngeal dyspnœa on arrival, intubated one half hour later; large piece of thin, crumbling membrane coughed up through tube; swollen tonsils, with small whitish patches. Temperature, 99.4° F.; pulse, 104; respiration, 26.

March 24th. Tube removed; seems well; highest temperature, 101° F. No albumin in urine.

CASE V. April 27th. Male, aged forty-three. Died. On admission the history is obtained from friends that he has been three days sick. He is weak, slightly delirious, and appears as if suffering from some severe infectious disease. The whole uvula and the portions of soft palate adjacent to it are covered by a very thin, dirty covering which can hardly be called a pseudo-membrane. The whole pharynx and palate are extremely hyperæmic. Patient is hoarse, and has some laryngeal dyspnœa. Temperature, 103° F.; pulse, 128; respiration, 26. Patient became violently delirious, and died the next day. No autopsy.

This case is interesting, as it is the only fatal one in adults. It is probable that the croupous inflammation was only a complication of some one of the infectious diseases.

Summary.—These typical cases prove that membranous croup is at times an independent disease, having no connection with true diphtheria. In only 2 out of 16 investigated by me was any connection with scarlet fever or measles discovered. A diagnosis from the clinical history and appearance is impossible. Of the 16 cases there were 6 deaths.

In the majority of the 10 cases that recovered the course of the disease was mild. After intubation had relieved the dyspnœa the patients never appeared dangerously ill. By the third day they were sitting up in their beds and playing with their toys. The temperature averaged somewhat higher during the first days than in the cases of laryngeal diphtheria, and rose to 103° and 104° F. when the lungs became involved.

In 2 of the children a pretty clear history of direct infection from other cases was obtained. In non-diphtheritic croup the magical effect of intubation is seen, for without tracheotomy or intubation the majority would certainly have died. The percentage of recovery was 71½ per cent. in the cases not complicated by scarlet fever. Broncho-pneumonia was the most frequent cause of death.

3. *Pseudo-membranes confined to the Tonsils caused by Streptococci.*—CASE I. March 3, 1892. Female, aged six. Clinical history: From an asylum with 3 other cases. Right tonsil is swollen and covered by a thick, adherent, gray-colored, fibrinous pseudo-membrane. Cervical glands considerably swollen on right side; slight pain and tenderness. Temperature, 101° F.

March 5th. Still thick membrane on tonsil, nowhere else. Feels well.

March 7th. Tonsil clean. Is slightly croupy.

March 9th. Perfectly well.

CASE II. Male, aged four. From same asylum. Clinical history:

Pseudo-membrane on upper portion of left tonsil and adjacent surface of anterior and posterior pillars. Well on third day. No fever.

CASE III. March 5, 1892. Female, aged twenty-one. Clinical history: Both tonsils are nearly covered by irregular, semi-adherent pseudo-membranous patches. Considerable swelling and hyperæmia. No swelling of glands. Not much pain; slight constitutional symptoms. Temperature, 101° F.

March 7th. Tonsils nearly clean. Feels well.

March 8th. Perfectly well.

In adults thick croupous patches, adherent or non-adherent, if confined to the tonsils after twenty-four hours, very rarely have anything to do with true diphtheria. The same bacteria (the streptococci) which under certain influences cause an inflamed throat or a follicular tonsillitis, under others seem to produce a croupous tonsillitis. Two members of a family may be affected, one with the former, the other with the latter disease. In a few cases a very complete history of direct transmission of the contagium is obtained. The croupous deposit or pseudo-membrane lasts from two to seven days. All cases recover without complications.

The intimate connection of some cases of croupous tonsillitis with scarlet fever is brought out in the following example:

Female, aged twenty-one, was admitted to the hospital with marked croupous tonsillitis, with constitutional and local symptoms, on May 20th. The three previous days she had taken care of a child sick with scarlet fever, and on the last day also of the mother, who was attacked with croupous tonsillitis. Both she and the mother had come in frequent direct contact with the child.

Two physicians attended a gentleman sick with malignant scarlet fever and croupous tonsillitis. Both were attacked with croupous tonsillitis, and one with scarlet fever also.

PROGNOSIS.—With the exception of cases in which the larynx is involved uncomplicated cases of pseudo-diphtheria are not dangerous to life. Although non-diphtheritic croupous laryngitis is less dangerous than diphtheritic, still the danger of suffocation without operative relief and of complicationg pneumonia is ever present, and the mortality is considerable.

Pseudo-diphtheria complicating infectious diseases during their early stages adds somewhat to the danger of the disease, and is usually an indication of a severe infection.

TREATMENT.—The treatment of pseudo-diphtheria is similar to that of equally severe cases of diphtheria, with the exception of the antitoxin.

In cases not involving the larynx the temperature, general pains, and local soreness can be somewhat alleviated by giving internally salol gr. v every three to six hours or phenacetin gr. v every six to eight hours in adults, gr. iii in children. Antipyrine, antifebrin, and salicylate of soda are also employed with good effect in the tonsillar cases.

PERTUSSIS.

BY J. P. CROZER GRIFFITH, M. D.

SYNONYMS.—Whooping cough; Tussis convulsiva.

DEFINITION.—An infectious disease, occurring principally in children, and characterized by a cough of a peculiar paroxysmal nature and by more or less bronchial, laryngeal, and nasal catarrh.

ETIOLOGY.—*Age.*—Among the most powerful predisposing causes of whooping cough age would seem to hold a prominent place. The great majority of cases occur before the sixth year, and over half of these before the fourth year, according to the estimates of West. Before the age of six months the disease is not so common, although less unusual at that period of life than are scarlet fever, measles, and some of the other infectious diseases of childhood. In a few reported cases it seems to have developed before birth. It does not often occur after the age of ten years, although adults sometimes are attacked by it. The chief cause for this immunity of adults doubtless is that the majority of them suffered from the disease during childhood. There is, however, probably a lessened susceptibility to it with advancing years.

Sex does not appear to exert any decided etiological influence. It has often been stated that pertussis is more common in girls than in boys, but the truth of this does not seem to be entirely confirmed by statistics, which are not at one upon this point. The extensive statistics of Vladimiroff favor the greater frequency in girls.

The state of the *previous health* is important. It is the general opinion that weakly, delicate, or sickly children acquire whooping cough more easily than do those who are well. An attack of measles is often followed by one of pertussis. This association is especially well illustrated in epidemics of the two disorders. Indeed, the statement is often made that an epidemic of measles predisposes to the development of one of whooping cough. It does not seem clear, however, whether the association is only accidental or whether it is actually etiological. Whatever causal relation other diseases may have to whooping cough, it appears certain that its development is not at all hindered by their existence.

Climate, *season*, and *geographical position* do not seem to exert any real influence. The disease, it is true, is more prevalent in the civilized parts of the world, but this depends merely on the fact that it has not yet been carried to other regions or has not yet become firmly established there. There are contradictory statistics regarding the frequency of the disease at any one period of the year, which show that season certainly has but little bearing.

The *station in life* is likewise without much influence. The poor are

rhaps more subject to it, on account of the greater ease of its diffu-
n which their unhygienic method of living occasions.

The exciting cause of whooping cough is infection. Consequently,
disease occurs in epidemics, although in the larger cities it is practi-
ly endemic. The epidemics seem to have a disposition to appear at
ntervals of about two years. The virulence of the infectious principle
so great that nearly all children exposed to it will contract the dis-
e. The infection is transmitted by the breath and by the secretions
m the respiratory tract. Comparatively close contact is required,
hough this need be of but very short duration. Probably the poison
nters by way of the respiratory tract, but it is not certain that this is in-
ariably the case. It is possible for the disease to be carried by a third
erson from the sick to the well by means of handkerchiefs, clothing,
and the like; but this is certainly of very rare occurrence. The infectiousness of whooping cough is present during the whole of the attack, but especially in the paroxysmal stage.

PATHOLOGY.—The nature of the infection, as indeed the nature of the disease itself, is not definitely understood. It is not even admitted by all writers that the disease is of an infectious nature. De Mussy claimed that it is due to the irritating pressure of enlarged bronchial glands upon the terminal filaments of the pneumogastric nerve. Other writers have advanced the theory that it is of the nature of a pure neurosis, the result of some functional disturbance of the pneumogastric, recurrent laryngeal, phrenic, or sympathetic nerves, or of the medulla. Still others have thought it to be a simple bronchial catarrh associated with a neurotic condition. The whole analogy of the affection to diseases of the infectious class indicates, almost beyond question, that it too belongs to this class. Various organisms have been supposed to be the cause. The larvæ of insects were assigned as the active agents by Linnæus. Bacteria were described by Poulet and by Letzerich, and a protozoön was found in the sputum by Deichler. The observations which have been the most promising are those of Afanassiew, who isolated a short bacillus from the sputum of pertussis patients which he named the *bacillus tussis convulsivæ*. He was able to obtain pure cultures of this which, inoculated upon the respiratory mucous membrane of animals, produced some of the symptoms of whooping cough, with a catarrhal state of the respiratory tract and a tendency to broncho-pneumonia. Moncorvo has also described a bacillus found in the sputum, and more recently Ritter has found a small coccus which he believes to be the germ. It is evident that further research is greatly needed in this direction.

The manner in which the germs of the disease, whatever they may be, produce the symptoms is also by no means clear. It is possible, on the one hand, that they act primarily upon the respiratory tract, occasioning a catarrhal inflammation, or, on the other hand, that the nervous system is primarily affected. There is no question that a catarrhal condition of the respiratory tract is present in whooping cough. Some writers have claimed that this is most marked in the nose, others hold that it is predominant in the bronchi. It would seem from the observations of Meyer-Huni and of Von Herff that the mucous membrane of the nose, larynx, and trachea down to the bifurcation is the region of the respiratory tract most affected. Of this the part which is pre-eminently involved is the "cough region"—*i. e.* the posterior wall of the larynx in the interarytenoid space. If we accept the view that the infection is chiefly local, with a secondary involvement of the nervous system, it would seem likely that a small quantity of mucus, rising from below, lands upon the cough region and sets up a powerful irritation of the hypersensitive filaments of the superior laryngeal nerve. This occasions, through reflex action, a series of repeated expiratory efforts which continue until the mucus is expelled. A long-drawn, crowing inspiration follows, due to a spasm of the glottis, itself dependent upon an irritation of the convulsive centres in the medulla. It seems very much more probable, however, that whooping cough is actually an infectious disease of the nervous system, with a secondary localization of the process upon the respiratory mucous membrane, exactly similar to the relation between measles and its respiratory symptoms. According to this view, some poison in the blood, produced by the infectious germs, occasions a great excitability of the superior laryngeal nerve or its centres in the medulla, and of other portions of the central and peripheral nervous apparatus which control respiration and cough. There are various grounds for this hypothesis. In the first place, the even occasional occurrence of pertussis shortly after birth as a result of fœtal infection indicates that the microbes must be in the general circulation. Then, too, paroxysms are brought on quite independently of the presence of mucus on the cough region. Thus excitement of any sort, drinking, crying, or sudden change of air will occasion them, all acting rather through the nervous system than in other ways. The greater frequency of paroxysms at night probably indicates the diminished degree of resistance of the respiratory centre in the medulla at this time, as a result of which convulsive respiratory efforts become more frequent. Of course, with this central excitability of the respiratory nervous system dependent on the infection, any local excitation, such as mucous or other irritant to the respiratory mucous membrane, will produce cough. The presence of pathogenic microbes on the respiratory mucous membrane might only indicate that this was the seat of entrance and chief seat of growth, and the disease would be in this respect exactly analogous to typhoid fever.

There are no characteristic post-mortem lesions. Emphysema is quite commonly found in bad cases, alone or combined with other pulmonary complications, especially broncho-pneumonia. Enlargement of the bronchial glands has been noted, but is not characteristic. Atelectasis is a common condition.

SYMPTOMS.—The attack is ordinarily divided into four periods: (1) incubation; (2) invasion, or the catarrhal or premonitory stage; (3) the paroxysmal or whooping stage; and (4) the terminal stage or stage of decline. There is no very sharp division between these, since they pass gradually into each other.

(1) *Incubation.*—During this period no symptoms of the disease present themselves. Statistics are at variance regarding its length, and the fact that the invasion takes place so insidiously makes the determination of the exact duration of the incubation difficult in most cases. It probal lasts from two to seven days, with an average of three to four days.

(2) *Catarrhal Stage.*—At the beginning of this period there are present the evidences of a severe cold, such as slight hoarseness, obstruction to breathing through the nose, sneezing, tickling in the throat, a dry cough, and malaise. Although there is often some slight fever, especially in the evening, it is disputed whether this is merely the result of the catarrhal condition or whether it should be considered as the direct result of the action of the infectious poison on the nerve centres. Treatment may produce temporary amelioration in some cases, yet the tendency is for the symptoms to grow gradually worse in spite of it. This is especially true of the cough, which becomes more frequent, occurs in longer paroxysms, and is decidedly worse at night. Examination of the chest at this period shows either an entire absence of râles, or a number of them too insignificant to account for the severity of the cough. In a smaller number of cases there is a decided bronchitis during the premonitory stage, with numerous râles and considerable fever, but this is to be regarded rather as a complication. The premonitory stage lasts during a time which varies with different cases and whose exact length is difficult to determine, owing both to the insidiousness of its onset and the fact of its merging into the next stage. In some cases it continues but two or three days, while in others the whooping stage never comes on. The younger the child, the less in many cases is the length of the invasion. It may be said to average about two weeks.

(3) *The Paroxysmal Stage.*—The typical and fully developed paroxysmal cough of pertussis is marked by the occurrence of the "whoop," and it is customary to date the beginning of the paroxysmal stage from the time when this symptom first appears. A typical paroxysm of whooping cough, or a "kink," is very characteristic. Often it comes on very suddenly without any warning. In other cases some sensation just before the paroxysm warns the child that one is about to begin. This sensation varies with different children. It may be a tickling in the nose or larynx, or a strong inclination to cough, or a pain in the region of the sternum. If the child has been lying down, it sits up quickly and perhaps grasps at the side of the bed. If it has been playing about the room, it drops its toys and runs to its nurse or seizes upon any object near it for support. The cough then begins, and consists of a series of rapidily repeated, short, explosive expiratory efforts, followed by a long-drawn crowing inspiration. The short coughs are, as stated, little more than efforts at expiration, for auscultation reveals almost no sound of breathing, and only a series of impulses against the ear can be perceived. The expiratory efforts, without inspiration between them, continue for a few seconds, during which time the face becomes swollen and cyanotic, the eyes are prominent, congested, and watering, the tongue is protruded and driven against the teeth, saliva flows from the mouth, and the pulse grows rapid. The whoop which follows is the result of a spasm of the glottis. The ear against the chest wall at this moment hears at most a very feeble inspiration or none at all. Immediately after the whoop another series of expiratory efforts usually begins, and this alternation of expirations and whoop may be repeated several times. The whole attack lasts, as a rule, from a few seconds up to one or two minutes, but exceptionally it may continue for from ten to thirty or even more

minutes. In such a case, and often in the shorter attacks, momentary periods of rest occur, and then the coughing returns. In the latter part of a paroxysm ropy mucus may flow in abundance from the mouth, and vomiting is very apt to follow. In bad cases the paroxysms may be attended by hemorrhage from the nose or mouth or beneath the conjunctivæ, or even in the brain or elsewhere. The urine and fæces may be expelled by the violence of the coughing. Sometimes a whoop immediately precedes the first of a series of expiratory efforts. After an attack is over the child may be left pale and exhausted for a short time, but soon resumes its play if it is strong. Some degree of swelling of the face, cyanosis, puffiness of the eyes, and blueness of the tongue persists between the paroxysms and gives the child a very characteristic appearance.

The paroxysms are nearly always most numerous in the night. The number of paroxysms which occur in twenty-four hours varies greatly in different children. In the mildest cases there may be only six or eight, and these may occur almost entirely at night, leaving the child but little disturbed during the day. In severe cases, however, they may number forty or eighty, or even more, in twenty-four hours. A paroxysm is brought on by excitement of any kind, crying, singing, swallowing, exercise, the use of a tongue-depressor, a sudden change in the temperature of the air inhaled, the breathing of air vitiated by carbon dioxide, and so on.

Examination of the chest during the paroxysmal stage shows freedom from bronchitis, except perhaps of the slightest grade. Fever is absent or only occasionally present. If constantly present, some complication must be suspected. In mild cases the general condition of the child is unaffected, but in severe ones the nutrition and strength may suffer greatly from the frequent vomiting of the food taken and from the loss of sleep. The continuance of the paroxysmal stage is characterized by the occurrence of the paroxysms with unabated severity. Its actual duration is difficult to determine, and is very variable. It averages from three to six weeks, but may greatly exceed this.

(4) *The Stage of Decline.*—This is reckoned from the time when a distinct diminution in the severity of the disease can be observed. The preceding stage merges so gradually into it that its exact commencement can scarcely be determined. The paroxysms grow steadily less frequent and less severe. The cough has a much looser quality, and finally, although slowly, loses its paroxysmal character almost entirely, while the whoop becomes more and more infrequent. There is a muco-purulent bronchial secretion, and moist râles are heard in greater numbers in the chest. Hemorrhage and vomiting no longer occur. Finally, all whooping ceases and the disease changes into a simple bronchitis or the cough stops entirely.

The duration of this stage is even more variable than that of the two preceding ones. It ranges from ten days to several months. Should the winter season be approaching, occasional paroxysms with whooping may continue until spring, sometimes after all persistent cough has ceased. It not seldom happens that all cough disappears for some time, but returns again, even with whooping. Such a return cannot with reason be called a continuation of the third stage. It is often found that cough with whoop occurs at intervals for months or even during a year after the original attack began, being brought on even by slight bronchitis. The terminal stage may safely be said to have ceased when once cough has disappeared if only for a brief period, for whooping occurring after this is rather a habit than anything else, and is to be considered a pure neurosis without any infectious element.

COMPLICATIONS AND SEQUELÆ.—Complications connected with the respiratory apparatus are the most frequent. Bronchitis is very common, and when it develops early it may at first greatly obscure the diagnosis of the case. One of the most dangerous complications is bronchopneumonia. This is most apt to occur in feeble or rickety children or in those who have been subjected to exposure to cold or to improper hygiene of any sort. It is very prone to develop where measles has immediately preceded the attack of pertussis, but its most frequent cause is the occurrence of atelectasis. Atelectasis alone is a frequent complication in young children, especially in those who are weakly or rhachitic. It may be widespread or may be localized in a small area. Its onset is indicated by the ordinary symptoms of this disease, combined with a diminution or disappearance of the paroxysmal nature of the cough. Emphysema is a common complication, but is usually only temporary, although this is not always the case. Empyema, croupous pneumonia, and pleural effusion are of less frequent occurrence. Œdema of the glottis is not common. Hemorrhage from the nose is observed almost too often to be regarded as a complication. The same is true of hemorrhage from the mouth, but true hæmatemesis, in which the blood comes originally from the stomach and is not first swallowed and then vomited, is unusual. Hemorrhage under the conjunctivæ is frequent, but that from the ear or lungs or under the skin is rare. Meningeal hemorrhage is not at all uncommon, and is the cause of many instances of convulsions and cerebral palsy.

A superficial ulceration on and at each side of the *frænulum linguæ* is so common that it can almost be called a symptom. It is probably produced by the forcible driving of the tongue against the lower incisor teeth during coughing. It cannot be said to be diagnostic of whooping cough, for it may be seen in cases of severe cough from other causes. Loss of appetite, diarrhœa, and indigestion are frequent complications. The looseness of the bowels tends to be somewhat chronic, and the passages contain considerable mucus. Prolapse of the rectum, hernia, or involuntary evacuation of fæces may be produced by the violence of the cough. Convulsions constitute a not infrequent and a dangerous complication, often, as stated, the result of cerebral hemorrhage. General œdema of the skin and subcutaneous emphysema are very unusual occurrences. Hemiplegia, paralysis of other forms, persistent spasm of the glottis, aphasia, and sudden blindness are occasional complications. Albuminuria is quite frequent, and acute nephritis has repeatedly been observed. Sugar is sometimes found in the urine.

Other distinct diseases may accompany whooping cough or develop as sequelæ. Thus diphtheria, varicella, or other infectious disease may occur with it, but measles is especially likely to do so or still oftener to precede it. Rhachitis, anæmia, or other constitutional disease may be either a sequel or a complication. Tuberculosis is one of the sequelæ most apt to develop and most to be dreaded. It is liable to come on chiefly in children who have had pertussis very badly or whose general nutrition is much below normal from other causes. Its favorite seats, from which a more or less general affection may extend, are the bronchial and intestinal glands and patches of broncho-pneumonia. Various paralyses, blindness, deafness from rupture of the membrana tympani, epilepsy, aphasia, and disseminated sclerosis are among the numerous sequelæ which have occasionally been reported.

RECURRENCE AND RELAPSE.—Pertussis has a remarkable tendency to what appear to be relapses, yet which are not to be considered as such in reality. As has been pointed out, the return of whooping after the disease has apparently ceased is rather a neurosis than an evidence of a return of the disorder, since it is no longer infectious at this stage.

Recurrence of pertussis is extremely rare. Le Gendre was able to collect only 8 cases in addition to 1 seen by himself.

DIAGNOSIS.—In the early stages the diagnosis of whooping cough is difficult or impossible. The existence of a cough which becomes more and more paroxysmal as time passes, in spite of treatment directed to a possible bronchitis, renders the existence of pertussis very suspicious, especially, too, if physical examination does not reveal a bronchitis which is at all commensurate in severity with the intensity of the cough. Vomiting occurring after the paroxysms of coughing and the greater frequency of the attacks at night are also diagnostic points. Of course the prevalence of an epidemic of the disease or the existence of other cases in the family are additional confirmatory signs. The development of the whoop will settle the matter finally, except in those cases where the disease never passes the catarrhal stage. In these cases the occurrence of vomiting, the congestion of the eyes, and the character of the cough are often sufficient to render a diagnosis possible; but it is especially in such cases that the prevalence of the disease as an epidemic or its existence in other members of the family renders the most valuable service in determining the nature of the attack.

Sometimes a severe acute bronchitis with an unusually spasmodic cough greatly resembles pertussis, but the existence of decided fever, shortness of breath, and numerous râles in the chest generally serves to distinguish it. The difficulty is especially great at the close of an attack of measles. Here we have, on the one hand, the existence of a severe bronchitis which may appear to account for the severity of the cough, and, on the other hand, the tendency which pertussis has to appear after an attack of rubeola. Broncho-pneumonia is most liable to develop in the later stages of pertussis. When it occurs during the catarrhal stage it may alter the character of the cough and even prevent entirely the development of the whoop, making the diagnosis difficult. A prolonged terminal stage of pertussis may simulate tuberculosis of the lungs. Only continued observation of the case will render it possible to determine whether this disease is actually developing. Tuberculosis of the bronchial glands may occasionally be the cause of a paroxysmal cough which greatly resembles that of pertussis. The long continuance of the affection, the absence of distinct stages, of vomiting, and of very characteristic whooping, and the history of previous wasting and of fever, serve to distinguish it.

PROGNOSIS.—The danger of whooping cough is far greater than is commonly supposed. Statistics show that a very large number of children die of it. For instance, J. Lewis Smith states that 4840 deaths from it occurred in New York City during a period of fifty years, this equalling 1 out of every 79 deaths from all causes. W. W. Johnston says that an estimate based on the census of 1880 shows that over 100,000 children died of whooping cough in the United States during ten years: 120,000 persons fell victims to it in England and Wales between 1858 and 1867, and 85,000 in Prussia between 1875 and 1880. Not only is the actual number of deaths large, but the proportion of fatal cases to the whole number of cases is very considerable. Statistics would indicate that the relative mortality is from 3 to 15 per cent., and occasionally higher. The mild cases of course recover, and it is upon the complications that the mortality largely depends, although in severe uncomplicated cases death may be caused by the great exhaustion produced or by other ways. The younger the child the greater is the danger to life. After the age of five years few succumb, while under that of two or three years the death rate is at its highest. Rather more females die than males, probably the result of a less degree of strength of constitution and of resistance possessed by them. Badly nourished children raised amongst unfavorable hygienic surroundings naturally suffer the most. Any constitutional disease, such as rickets, increases the danger. The previous occurrence of measles just before the development of pertussis renders the prognosis much graver. Both the summer and the winter seasons bring their dangers with them. In the first the occurrence of intestinal complications and the debilitating influence of hot weather add to the danger, while in the latter the liability to the development of respiratory disorders distinctly increases the risk. Broncho-pneumonia complicating pertussis makes the prognosis most grave and is a common cause of death. Convulsions, too, constitute a common fatal ending. Tuberculosis occurring as a sequel adds greatly to the death rate.

TREATMENT.—*Prophylaxis.*—In the light of the danger and the great infectiousness of pertussis every effort should be made to guard children from the disease. The custom so prevalent of allowing children suffering with it to play freely with others in the streets or parks cannot be too strongly condemned. Children should be strictly kept from the slighest contact with those who are even suspected of having whooping cough, since it is infectious in the catarrhal stage as well as later. Unfortunately, the difficulty of recognizing the malady at this period renders the task almost herculean. Where an epidemic is prevailing it is better to remove unaffected children entirely from the locality. This is especially true in the case of weakly or very young subjects.

It is impossible to determine exactly how long infectiousness continues. It grows less during the last stage, and it may ordinarily be assumed to have ceased entirely by the end of two months after the onset of the disease. Quarantine may be discontinued after the child has ceased to cough for a few days, even though coughing return, with or without the whoop, afterward. As has previously been remarked, this later coughing is rather a neurosis or of a purely catarrhal nature than in any way partaking of the original infectious character. Both in the cases in which the cough returns at intervals for months and in those in which one or two paroxysms daily persist for an indefinite time it would be as clearly entirely impracticable to continue quarantine as it would be unnecessary. In such cases isolation may cease two or at most three months after the onset. Since there is a possibility, although a remote one, of transmitting the infection by the bed- or body-linen, disinfection of this should be carried out, as well as of the room, after the disease is over.

Treatment of the Attack.—In the treatment of pertussis the physician often encounters a problem which taxes his resources and ingenuity to the utmost. The mildest cases require only careful supervision or are easily relieved to a very satisfactory extent by medication. In the severe cases, on the other hand, the condition is far different. Here we must be ready to employ one plan of treatment after another until something of benefit is found, for there is no disease of which it is truer than of pertussis that the treatment which has acted like a charm in one case or series of cases may fail utterly in another series or individual. Even in one family one child may be greatly relieved by one drug and another only by another. Then, too, we must not fail to employ our remedies in sufficiently large dose before decrying them as useless. So also it is only early in or at the height of the disease that we can come to any conclusion regarding the virtue of any plan of treatment, for almost anything will seem to benefit when the attack is about to undergo its natural decline.

Treatment may be conveniently divided into—(1) hygienic; (2) local; (3) general.

1. *Hygienic treatment* is of great importance. Children who are not suffering from any respiratory complication should be kept in the fresh air as much as possible. There is no doubt that air vitiated by carbon dioxide increases the number and intensity of the paroxysms. On the other hand, they must not be recklessly exposed, since the tendency to respiratory complications is so great. Damp and windy weather must be avoided and the children confined in airy rooms. It is an excellent plan to have two large rooms—one for the day and the other for the night—and to air each thoroughly before it is used. The number of paroxysms at night is often considerably diminished in this way. Clothing must be sufficiently warm, and food should be nutritious and easily digestible, and given frequently in small quantities in cases where the tendency to vomiting is troublesome. Nutrient enemata may be required in some of these cases. Change of climate often works wonders, especially in the stage of decline. It should, however, never be employed at the expense of unaffected children.

2. *Local treatment* has been largely employed. It may be divided into (*a*) insufflation of powders into the nose or larynx; (*b*) applications of solutions by the spray or brush or by irrigation; (*c*) inhalation of volatile substances and of gases.

(*a*) Quinine by insufflation has been one of the most popular methods of local treatment. The formula first recommended by Letzerich consisted of a mixture of this drug, bicarbonate of soda, and powdered acacia. With this insufflations were made into the larynx three times a day. Very excellent results with quinine have been obtained by a number of icians. Laryngeal insufflations are not easy to employ in the case of ung children, and it is quite certain that in the hands of any one not pecially skilled in the manipulation the greater number of them never each the larynx at all. On this account nasal insufflations of quinine re to be preferred. Among the other powders which have been recommended for insufflation into the nose or larynx are resorcin, boric acid, nzoin, iodoform, salicylic acid, borate of soda, antipyrine, and tannin. these benzoin appears to hold the most prominent place and to have most authority in its favor. Boric acid is also serviceable in many cases. I have found it useful by nasal insufflation, but the results were not so good as those obtained by internal medication. Resorcin is also hly praised. Guttmann recommends sodium sozoiodol for nasal ufflations. Various combinations of powdered drugs for insufflation have been recommended by different writers. Thus, boric acid and powdered coffee are praised by Guerder, and benzoin, salicylate of bismuth, and quinine by Moizard.

(*b*) One of the earliest methods of local treatment for pertussis was the application of a weak solution of nitrate of silver to the larynx, recommended by Watson in 1849. Some later observers have obtained good results with it. A solution of cocaine of a strength of from 2 to 15 per cent. has been used as an application to the pharynx by the brush or spray. It can undoubtedly do good, but the effect is liable to be only transitory and the remedy is not devoid of danger. Alarming symptoms produced by the application have been reported. Among the other drugs in solution which have been used locally as a spray or on the brush are peroxide of hydrogen, morphine, resorcin, bromide of potassium, chloride of ammonium, alum, tannic acid, and salicylic acid. Resorcin is one of the best of these. It has been especially recommended by Moncorvo, who applies it in 2 per cent. solution with a brush to the larynx once daily. Irrigation of the nares is advocated by numerous writers. For this purpose we may use peroxide of hydrogen, a saturated solution of boric acid, sulphate of iron in the strength of 1 grain to the ounce of water, bichloride of mercury, 1 : 6000, and salicylic acid, 1 : 1000. The procedure is very unpleasant to the child, is not devoid of danger to the Eustachian tubes, and is not in any way superior to insufflation or atomization.

(*c*) Desmartes in 1859 first recommended the inhalation of the air from the purifying rooms of gas-works, and since then the value of the treatment has often been urged. Later studies have not sustained the claims which have been made. Among the numerous other substances recommended for inhalation are carbolic acid, creasote, eucalyptus, turpentine, terebene, tar, petroleum, thymol, pumilene, benzine, camphor, ozone, naphthalin, nitrite of amyl, and compressed air. Of these the one which would seem to be most generally esteemed is carbolic acid. This may be vaporized from a saturated solution in a croup-kettle or steam atomizer or from sponges or cloths wet with it and hung about the room, or it may be inhaled from a respirator placed over the mouth and nose. It may also be volatilized by placing a few crystals upon hot iron. The fumigation of the room with burning sulphur was strongly advocated by Mohn, and his experience has been confirmed by others. The sulphur should be burned after the child has been removed in the morning and dressed in clean clothes. After five hours the room should be well aired, and then slept in that night. Inhalation of chloroform or ether has been advised for its anæsthetic effect.

3. *General Treatment.*—Inasmuch as the disease appears to be due to a disordered condition of the nervous system dependent upon a systemic infection, much is to be expected from internal medication—more, I think, than from local treatment. The method to be followed depends somewhat upon the stage of the disease. Early in the attack, before the paroxysmal character of the cough develops, remedies useful in bronchitis may be selected. Late in the attack, when secretion becomes more abundant, expectorants may be indicated, or, if the secretion is very profuse, medicines to hold this in check to some degree. Throughout the whole course of the disease, however, the neurotic nature of the cough generally makes it necessary to use remedies chosen for their quieting effect upon the nervous system. In the mildest cases, in which the paroxysms do not exceed four or six in twenty-four hours, are not very severe, and have no influence upon the general health, it is often just as well to refrain from any medication or to use only such as will aid in procuring quiet nights.

So many remedies have been proposed that it is impossible to review all of them; only those which seem to have oftenest been of avail can be discussed. The testimony of many investigators shows that antipyrine is one of the drugs upon which most reliance can be placed. It was first recommended for this disease by Sonnenberger. It must be given in sufficiently large doses and its use must be persisted in; and it may be said in this connection that children take it in proportionately larger doses than adults do. Beginning with a small amount, this should be rapidly increased until a child of two years is taking 2 or 3 grains every three hours. In afebrile states it is never depressant unless some idiosyncrasy exists. In many cases its action is little short of marvellous, but in the majority all we can expect is a decided lessening of the number and severity of the paroxysms. Phenacetin, acetanilid, and other remedies of this class may be used in place of it, but the effects do not seem, as a rule, to be so good. Sometimes one drug of this class will be of service when another has failed.

Bromoform, recommended by Stepp, has proved of value in the hands of many observers. It may be given in doses of from 2 to 4 drops three or four times a day at three to six years of age. It is most conveniently administered on moistened sugar or in a mixture with alcohol, in which it is soluble. My own results have been favorable in many instances, although not as often so as with antipyrine. Sometimes bromoform makes the child sleepy and stupid without affecting the severity of the disease, and in a few instances it has seemed to be dangerous. Belladonna has been used for years, and is of undoubted service in many instances. It often needs to be given in large doses. A child of two years should begin with 2 minims of the tincture or $\frac{1}{12}$ grain of the extract three or four times a day, and have this increased until the limit of tolerance is reached. Quinine is another drug whose value has been proven beyond doubt. Large doses are required: 1 grain or more may be given every two to four hours at two years of age. Its taste may be partially disguised by syrup of liquorice or of yerba santa, or it may be given by suppository. If it disturbs the digestion, its use should be discontinued. Opium is one of the most valuable of drugs in many instances. In light cases it is often very servicable in small doses given during the day. In severe cases it is sometimes unequalled in full doses, given at night to produce sleep and allay the cough. Bromide of potassium is often very serviceable in doses of 2 to 5 grains at two years of age, repeated as needed. It may be advantageously combined with antipyrine or belladonna. Chloral is another drug which is frequently of value, especially for procuring sleep at night. The dose at two years should be from 1 to 3 grains. That it is a cardiac depressant must not be forgotten. Alum has long been a favorite; it is especially useful to check excessive secretion in the later stages, or when the presence of the mucus seems to excite the paroxysms: 2 grains may be given every three or four hours at two years of age. Among other drugs which have been recommended, and for the value of which there appears to be distinctly favorable evidence, are cannabis indica, castanea, drosera, asafœtida, quebracho, carbolic acid, creasote, peroxide of hydrogen, ouabaine, terpene hydrate, wild thyme, grindelia, pilocarpine, resorcin, camphor, hyoscine, turpentine, benzol, carbonate of iron, and conium. The use of the galvanic current has also been recommended. Several observers have made the statement that vaccination modifies greatly the course of whooping cough. In some of the cases coincidence may have much to do with the apparent action of the vaccine infection. In others it is readily possible that one disease may have modified the course of the other. Further studies upon the question are needed.

EPIDEMIC PAROTIDITIS.

BY J. P. CROZER GRIFFITH, M.D.

SYNONYMS.—Parotitis; Mumps.

DEFINITION.—Epidemic parotiditis is an acute infectious disease, characterized by inflammation of the parotid gland, sometimes with involvement of the other salivary glands, and occasionally of the testicle, the mammary gland, and the female genital organs.

ETIOLOGY.—Mumps is rare in children under two years of age, and is commonest in those between five and fifteen years. Young adults are also strongly predisposed to it. Old age is almost always exempt. It is generally considered that sex exercises a powerfully predisposing influence, and that males are much oftener attacked than females.

The season of the year is an influential factor. The statistics of Hirsch have been confirmed by later experience, and show that it is the colder months in which mumps especially prevails. Climate appears to possess little etiological power, and the same is true of geographical regions. It is true that certain localities may suffer from epidemics of mumps year after year, while others remain free, and that the latter may suddenly and without apparent reason become subject to it. The disease is of a decidedly epidemic nature. The epidemics are oftenest limited to a house or street, or consist of outbreaks in barracks or camps, but sometimes they are widespread over a city or even a district of country. In such cases it has frequently been observed that the disease spreads very slowly from house to house. It does not become prevalent over a large district at once. An epidemic may last for months or may be short-lived and attack but few individuals.

As with other diseases of a similar nature, however, the sole real producer is infection, the contagious principle being transmitted from the sick to the well. In just what way the infection takes place is uncertain. The frequent limitation of the disease within narrow confines indicates that the poison cannot be one which is easily disseminated, and that it probably can be communicated only by close contact with an infected person, it being transmitted either in the breath as expired or in the secretions from the mouth, and being taken in through the mouth of the person acquiring the disease. It would also seem very probable that it can be carried in the clothing of a third person. The infectiousness is certainly present during the actual existence of symptoms, and even after these have disappeared. There are numbers of reported cases also which indicate that the disease can be transmitted even during the stage of incubation. The degree of infectiousness seems to depend largely upon the closeness and the frequency of the contact. Thus breaks in barracks or other public institutions the disease is liable attack a large proportion of those exposed.

PATHOLOGY.—The true nature of the malady is far from being erstood. It is not even decided whether it is to be considered a l infection upon which the fever and other symptoms depend, or a neral blood infection with a secondary localization upon the salivary nds. Analogy to other infectious diseases would indicate that the last pothesis is the correct one. The occasional involvement of other ore remote glands, as the testicle, also certainly favors this view, as does the existence of a period of incubation, although it is possible that the germs may be lying dormant or developing in the duct of Steno during this time.

It is fair to presume that some micro-organism is the active infectious agent of mumps, but the na the microbe is still a matter of which nothing positive is known. Capitan and Charrin, whose investigations have been among the mo mportant, found bacilli and micrococci in the blood and saliva of a number of patients with mumps. They were able to make cultures of these, but did not find them pathogenic for animals experimented on. Ollivier has discovered the micro-organisms in the saliva, urine, and blood, and Bouchard in the saliva and urine. The observations have been confirmed by Netter, Vedrenes, Boinet, and Bordas. Laveran and Catrin discovered a diplococcus in 67 out of 92 cases. This was present in the blood and in the secretion from the parotid gland. It was also obtained from the testis in cases of orchitis. Inoculation experiments were negative in their results. Whether the various micro-organisms described by these different observers have any etiological significance cannot yet be determined.

The pathological anatomy of mumps is little understood. The fact that the course of the disease is always benign or that fatal cases are complicated interferes with satisfactory post-mortem examinations. The swelling is situated in the parotid glands in most cases, but sometimes in other salivary glands as well or alone, or in the testicles alone. Cases have been reported in which the submaxillary glands were first affected, and then the testicles, while the parotid glands were at no time attacked. The periglandular tissue is also involved. Virchow described the process as a catarrh of the epithelium of the salivary passages in the gland. Others have considered the swelling to be the result of exudation of serum into the gland or the periglandular tissue. Bamberger found an inflammatory exudate in the interacinous connective tissue.

SYMPTOMS.—*Incubation.*—The period of incubation is a somewhat variable one, and different estimates of its length are given. In general it would seem to vary between one and three weeks, with an average of about two weeks. Nicholson reports an instance of the incubation lasting six weeks, and periods as short as three or four days have also been known (Leitzen). There are, as a rule, no symptoms during this time.

Initial Stage.—In the majority of cases prodromal symptoms are not present or are overlooked, and the enlargement of the gland is among the first symptoms. In other cases, however, there is a distinct period of invasion. The frequency of the occurrence of prodromal symptoms seems to vary with different epidemics. Young children exhibit them much oftener than adults do. These symptoms when well developed consist of malaise, chilliness, headache, general neuralgic pain, disturbed sleep or somnolence, loss of appetite, and moderate fever. In some epidemics there are also vomiting, diarrhœa, and, in young subjects, convulsions. Not all of the prodromal symptoms will appear in any one case. Rilliet and Barthez state that prodromes were present in 1 out of 3 cases occurring sporadically in their hospital practice. The prodromal symptoms last a few hours to perhaps two days. In exceptional cases they may continue four to eight days.

Stage of Swelling.—Generally by the second or third day after the beginning of symptoms evidences of involvement of the parotid gland appear—if, indeed, as stated, they are not the first signs of the disease. A dull, aching, continuous pain begins in the region of the ear and cheek on one side. It is made worse by pressure and by every movement of the jaw for eating or speaking. It hinders to a considerable extent the opening of the mouth, and often renders it impossible. Pain in the ear is not uncommon. Swallowing and the movement of the head are often painful. The degree of pain, slight at first, increases gradually during several days, coincidently with the increase of swelling. Its intensity varies with the case. Sometimes it is but slight, and may even be almost wanting, except upon movement of the jaws, while in other cases it is constantly severe. Rilliet and Barthez have described three especially painful points as being very frequently present—viz. on the mastoid process, on the temporo-maxillary articulation, and over the submaxillary gland. Swelling commences a few hours after the first development of pain and increases rapidly, reaching its height by the second to the fourth day, or sometimes not until the sixth day. It begins in the region of the parotid gland, between the descending portion of the lower jaw and the mastoid process. Although it may remain confined to this area, it often spreads backward, forward, and downward owing to the involvement of the submaxillary and sublingual glands, the connective tissue of the face and neck, and the cervical lymphatic glands. The ear seems lifted up and pressed outward, and, in cases of extensive swelling the outline of the lower jaw disappears and the whole side of the face and neck seems much swollen. The skin over the swelling usually is pale and shining. Only seldom is it reddened. Pressure with the finger generally meets with an elastic resistance, but when there is much œdematous infiltration of the skin pressure is very painful and leaves an indentation. In cases of very extensive swelling the œdema may extend even to the upper part of the chest. After the swelling has reached its height the diminution in size begins. The rapidity with which this occurs is very variable. Generally no trace of it remains by the seventh or eighth day after its first appearance, although it occasionally persists a longer time.

In the majority of cases both parotids are attacked, but it is only exceptionally that the swelling in them comes on simultaneously. According to some writers, the gland of the left side is usually the one first swollen. The second parotid is involved one or two days after the first begins to enlarge. Sometimes the interval is longer, and it may happen that the disease has nearly disappeared from the first side before it shows itself on the second. Almost always the second swelling is less pronounced than the first.

ver of varying degree, mentioned among the prodromal symptoms, nues during the stage of swelling, its height depending largely n the severity of the attack. As a rule, it is slight, with morning issions and evening exacerbations, and it gradually rises until it hes its height, generally not much more than 102° F., with the maxi- n of the swelling. Then it falls rapidly to normal. Occasionally, ially in severe cases, the temperature rises higher than this, and continue in the neighborhood of 104° F. for several days. The se and respiration maintain their normal ratio to the temperature. Some degree of malaise and prostration may be present. Redness the fauces and lining of the cheeks and severe tonsillitis are some- es observed. Ringing in the ears and some deafness are not uncom- on during the height of the disease. The secretion of saliva is ometimes increased, but is oftener diminished. Gerhardt found by introducing a cannula into the duct of Steno that the saliva from the affected gland came more slowly than normal, but exhibited no material changes in character. The pressure of the swollen glands narrows the fauces and increases the difficulty in swallowing, makes the voice nasal, and may cause dyspnœa by pressure on the larynx. Œdema of the larynx is sometimes produced. Vomiting, diarrhœa, and epistaxis are occasionally seen. In the form of the disease sometimes called the typhoid type there is a prominence of threatening nervous symptoms, such as delirium, restlessness, adynamic state, and involuntary evacuations. Enlargement of the spleen often accompanies the severe cases.

One of the most interesting of the symptoms of mumps—too integral a part of it to be called a complication—is the involvement of the genital apparatus, especially the testicle. This was once considered to be the result of metastasis, the transmission to the testicle of some poisonous substance produced in the parotid gland. The fact that occasionally the testicle is the first to be affected or, as in the cases reported by Kovacs and others, is alone involved, proves that this theory is incorrect and that orchitis is simply a localization of the specific poison upon the testicle. The severity of the parotiditis seems to have no influence on the tendency to orchitis. The involvement of the testicle is very rare in children. It is oftenest seen in youths and young adults, but here, too, its frequency varies greatly with different epidemics. Laveran reports it as occurring in 1 out of every 3 cases among patients in the army, while the observations of some others place its frequency at much less than this: 699 cases of mumps occurring in 14 different epidemics, collected by Comby, gave 211 cases of orchitis, a percentage of 30. As a rule, orchitis begins six to eight days after the appearance of the parotid swelling. In the majority of instances only one testicle is attacked. In the cases where both suffer the inflammation begins in the second from two to four days after the first is affected. The process is a true orchitis, and the epididymis is only occasionally involved, and then generally to a less degree.

The symptoms of the testicular involvement consists in a renewal of the fever, which had grown less or disappeared, but which now reaches 101° F. or more. Not infrequently severe or even threatening symptoms attend or precede the process, such as vomiting, severe diarrhœa, rapid, feeble pulse, profound depression of strength, delirium, and typhoid symptoms. There is dull or severe pain in the testicle with swelling and tenderness. The skin of the scrotum is red and tender and sometimes œdematous. The inflammation reaches its height by the third or fourth day, continues severe from two to three days, and then rapidly grows less. The severe general symptoms usually diminish rapidly by the time the testicular swelling has appeared, but the fever continues high until the enlargement of the gland has diminished, when it descends by crisis or by lysis.

Most cases of orchitis recover entirely, but atrophy sometimes results. In certain epidemics the proportion of cases atrophying has been very high. Very exceptionally an analogous inflammation is seen in females, affecting the ovaries, external labia, or mammary glands.

COMPLICATIONS AND SEQUELÆ.—In very rare cases suppuration of the parotid gland takes place or a chronic induration with some enlargement may remain for a long time. Suppuration of the testicle has also occurred. Swelling of the lachrymal glands has been reported. This last, like swelling of the cervical and other lymphatic glands, is rather an unusual symptom than a complication, since it is analogous to the infectious orchitis. Albuminuria may be present in grave cases. Stomatitis is sometimes observed. Deafness arising during the disease has been alluded to. It may persist after the attack as a result of affection of the middle ear or even of the labyrinth. Influenza complicating mumps has been reported by Jackson, Fiessinger, and Currier. Paralysis from peripheral neuritis after mumps is recorded by Joffroy, and paralysis of accommodation by Boas. Insanity of various forms has been observed. The possibility of œdema of the larynx developing has already been mentioned. Among rare complications and sequelæ are nephritis, uræmia, hæmaturia, meningitis, convulsions, conjunctivitis, blepharitis, and other affections of the eye, coryza, otorrhœa, tonsillitis, œdema of the brain from pressure on the jugular veins, cystitis, vaginitis, urethritis, endo- and pericarditis, pneumonia, inflammation of the joints, etc.

RECURRENCE AND RELAPSE.—One attack of mumps gives almost certain immunity against subsequent ones. Very few instances of two attacks have been reported. Servier saw one case in which a second attack occurred five years after the first. Relapses are sometimes seen. Some instances of so-called relapse consist more in what might be called an exacerbation of the disease. In such cases the swelling of the parotid grows less on the second or third day, and then returns a day or two later. In other cases there is a genuine relapse, the swelling and other symptoms recommencing from one to two weeks after the first attack has entirely ceased.

DIAGNOSIS.—Although the diagnosis of mumps is generally easy to make, yet it is possible for mistakes to arise. A secondary parotiditis, developing, as it does, in the course of other affections, can be distinguished by its history, as well as by its symptoms. The swelling is unilateral, more painful, and probably finally becomes red and fluctuating, or it has a decided tendency to go on to suppuration.

Acute cervical adenitis is the condition most apt to be confounded with mumps. When either affection can be watched throughout its course the diagnosis is easy, but when a patient is seen for the first time th either disease already well under way, to distinguish between the o is often very difficult. Before suppuration has become evident in e inflamed lymphatic glands the swelling may extend over the edge the lower jaw and to the region of the parotid. Even now, however, e centre of the inflamed area seems to be rather below the jaw than ver the parotid, and as pus increases in amount and the inflammation oncentrates, as it were, about the lymph gland, the seat of the trouble ecomes very evident. In the rare cases in which mumps attacks primarily or solely the submaxillary gland the diagnosis from cervical lymphadenitis might be impossible early in the attack. Chronic inflammation of the lymphatic glands runs an entirely different course from mumps. In addition to this difference, any lymphatic inflammation covering so large an area is almost always multiple, and the individual enlarged glands can be detected by palpation. Diphtheria or scarlatina may be attended by swelling in the neck. Examination of the throat will reveal the local conditions there. Retropharyngeal abscess may extend until it involves the tissues in the neighborhood of the maxillary articulation. Digital examination of the pharynx will settle the diagnosis. Should mumps begin in or be confined to the testicle, the diagnosis from a simple orchitis might be impossible unless the existence of an epidemic of mumps was taken into account.

PROGNOSIS.—The prognosis of mumps is nearly always favorable, so far as life is concerned. The patient is, however, threatened by atrophy of the testicle, which is not an infrequent sequel of orchitis. There is, too, the occasional danger of permanent deafness remaining. Some of the other complications may in rare instances threaten life.

TREATMENT. — *Prophylaxis.* — The prevention of mumps is exceedingly difficult if not altogether impossible. This is due to the fact already stated, that the disease is probably infectious during the period of incubation, and that the infection can still be transmitted after symptoms have disappeared. It is safer, therefore, that patients suffering with mumps be kept from contact with others for three or four weeks after the first appearance of symptoms. Since close contact is required for the transmission of the disease, the extreme precautions for disinfection necessary with some diseases are not needed.

Treatment of the Attack.—In the majority of cases little treatment is required, although the patient should be confined to the house or bed. For the relief of pain hot fomentations or poultices may be applied or the face covered with raw cotton or rested against a hot water bag. The bowels should be opened by a mild laxative, preferably a saline. Fever may be combated by an ordinary febrifuge, or, in case the temperature is high, by antipyrine or other drug of this class, or by cold bathing. A preparation of opium may be needed if pain is severe and sleep much disturbed. Nourishment must be soft, since chewing is difficult or impossible. Adynamic symptoms may demand stimulants. The treatment of the orchitis does not differ from that proper for inflammation of the testicle due to other causes.

TUBERCULOSIS.

By WILLIAM OSLER, M. D.[1]

I. GENERAL ETIOLOGY AND MORBID ANATOMY.

DEFINITION.—An infectious disease due to the *bacillus tuberculosis*, characterized by the presence of nodular bodies called tubercles (or diffuse infiltrations) which may undergo caseation or sclerosis, and which may finally ulcerate or in some situations become calcified.

I. GENERAL ETIOLOGY AND MORBID ANATOMY.—(1) *Tuberculosis in Animals.*—In reptiles the disease is rare, though occasionally, as Sibley has shown, it is found in them in a state of confinement.

In birds the disease is common in the domestic fowls, but there are differences which warrant the separation of avian from other forms of tuberculosis.

In Domestic Animals.—One of the most important etiological facts in connection with the disease is its widespread occurrence in animals from which man derives a considerable share of his food. Bovines are chiefly affected. Recent studies and the improved methods of inspection have demonstrated the very widespread existence of the disease.

In the United States no compulsory systematic inspection is made at the abattoirs, but a good deal of information has been collected of late years. Of 5297 cattle slaughtered in Maryland, 159 were tuberculous (A. W. Clement), and of 15,506 animals slaughtered at the Brighton abattoir, near Boston, 29 were tuberculous (Burr).

Careful inspection of herds has been made in some of the States, and the tuberculin test employed to determine the presence of the disease. The New York State Commission examined 947 animals and condemned 66.

On the continent of Europe much more accurate statistics are available. Thus for the four years (1890–93, inclusive) the percentage of tuberculous animals among 132,294 oxen and cows slaughtered in Copenhagen was 17.7. At the Berlin abattoir in the year 1892–93, 21,603 animals out of 142,874 showed evidences of tuberculosis. In the same year 125 calves out of 108,348 showed signs of the disease. In Great Britain there are no satisfactory records to show the incidence of the disease in cattle.

In sheep the disease is very much less common. The percentage at Berlin is about 1.5. Horses are rarely attacked. Dogs and cats are not very liable to the disease. Cadiat has recently investigated carefully the subject of tuberculosis in the dog. At Alfort there were 40 cases disease among 9000 post-mortems. The disease, he states, orig-s usually in the intestines, and the virus is probably transmit- through bones which have been previously picked by tuberculous ients or the dogs have licked up what has been left on their plates. n one considers the very close contact of the dog as a domestic pet, somewhat remarkable that the disease is so rarely seen in it.

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[1] I beg to acknowledge the valuable assistance I have received in the preparation of this article from my assistants, Dr. George Blumer and Dr. T. B. Futcher.

n other animals kept as pets, such as the rabbit and guinea-pig, the ase, under natural conditions, is very rare. Both of these animals, vever, are very susceptible to the disease when inoculated. Among and monkeys kept in confinement tuberculosis is the most formid- disease with which these animals have to contend.

(2) *General Statistics of the Disease in Man.*—Tuberculosis is the st universal scourge of the human race. It prevails more particularly the large cities and wherever the population is massed together. It estimated that in civilized countries one-seventh of the deaths are due this disease. In the United States Census Report for 1890, 102,188 eaths were reported to be due to consumption. It is difficult to get accurate statistics as to the number of deaths due to other forms of the disease, but at a low estimate one can say that at least 150,000 persons die annually in the United States of all forms of tuberculosis. An estimation based on the Census Report gives the total number of persons in this country infected with tuberculosis as 1,050,000, or 1 in every 60 of the population (Vaughan).

The death rate from tuberculosis in the cities is very much higher than the average; thus Hirsch states that while the general death rate is 3 per thousand, that of Vienna is 7.7, and of Munich and Glasgow 4 per thousand.

Geographical position has very little influence. The disease is perhaps more prevalent in the temperate regions than in the tropics, but altitude is a more potent factor than latitude; in the high regions of the Alps and Andes and in the central plateau of Mexico the death rate from tuberculosis is very low.

The influence of race, which has been much studied, is probably less owing to any inherent differences than to the conditions under which the individuals live. The Indians of this continent are very prone to the disease. Matthews states that the death rate in the older reservations in the East was three times as great as that of the Indians still living in the Northwest. In this country the Irish and the negroes appear specially prone to the disease; on the other hand, the Hebrews possess a relative immunity. For the six years ending May 31, 1890, the average annual death rate from consumption in New York City, per 100,000 of population was—for the Irish, 645.73; for the colored, 531.35; for the Germans, 328.80; for the American whites, 205.14; and for the Russian-Polish Jews, 76.72 (J. S. Billings).

The interesting question arises as to whether tuberculosis is on the increase or on the decrease. E. F. Wells, who has tabulated an immense body of statistics on this subject, states that the evidence is in favor of a very positive decline in the prevalence of the disease. While the last decennial census of the United States does not show any decrease, yet in many of the larger cities there has been a striking diminution. The question has been considered very carefully by James B. Russell of Glasgow in his *Sanitary History* of that city. One or two of the sentences from his report may be quoted with advantage: "Between the five years 1870–74 and the five years 1890–94 there was a decrease of 41 per cent. in the death rate. If we start from the maximum period of fatality (1860–64), the decrease amounts to 44 per cent. The acceptance of the doctrine that every case of phthisis is the result of a specific infection—that, consequently, no one is foredoomed to have phthisis or any other form of tuberculous disease—gives great precision to our ideas of prevention." He attributes a good deal to the. diffusion of the knowledge that the existence and distribution of the tubercle bacillus is the first condition of infection, and also to the successful administrative efforts in securing "ventilation, especially of houses and byres; the removal of dampness by subsoil drainage and precautions adapted to the foundations and walls of houses; the abolition of dark spaces and enclosures; the dissemination of direct sunlight."

(3) *The Bacillus Tuberculosis.*—Although the researches of many workers, particularly those of Villemin, in the field of tuberculosis had left no doubt of the infective nature of the disease, it was not until the discovery of the bacillus by Koch in 1882 that the true nature of the parasite was known. In the fourteen years that have elapsed much work has been done on the bacillus tuberculosis in its various relations and from varying standpoints, but the original work of Koch was so thorough and far-reaching that our increase of knowledge has consisted in the elaboration of finer details, the essential facts remaining unchanged.

The Morphological and Biological Characters of the Bacillus.—The bacillus of tuberculosis is an aërobic, non-motile, strictly parasitic organism, capable under certain circumstances of growing without the presence of oxygen. Its length varies a good deal, ranging from 1 to 5 mikrons, or from one fourth to almost the entire diameter of a red blood corpuscle. The diameter varies very little, the average being about two tenths of a mikron. The organism may be either straight or more commonly slightly curved, and occurs very often in groups, the bacilli lying across one another. To within a comparatively recent period it was supposed that the bacillus of mammalian tuberculosis, in contradistinction to avian tuberculosis, did not show those peculiarities known as involution forms, but considerable variations, not only in length and shape of the organism, may occur, and even branched varieties may be seen, similar to those of the diphtheria bacillus. The question of spore formation cannot yet be said to be definitely settled. The small, refractile areas so commonly seen in stained specimens of the organism, and originally described by Koch as spores, certainly have not the characteristics of the ordinary spores, nor, on the other hand, have they the characteristics of mere vacuoles. It seems possible that these areas, though not really spores, may be, at any rate, particles in the bacillus which are more resistant than the rest of the organism, and which under certain circumstances are capable of developing into younger forms.

The Staining Reactions of the Tubercle Bacillus.—As Koch pointed out in his original article, the bacillus tuberculosis possesses peculiar staining reactions which are associated with it and with hardly any other

nism. These consist in the fact that the bacillus stained with great
ulty with the ordinary dyes, staining most intensely with alka-
e reagents, and that its resistance to decolorization was even greater
n its resistance to stain. Koch thought that this peculiarity was due
ibly to the membrane which surrounded the bacillus, which per-
ued the penetration of alkaline solutions, but was peculiarly resistant
the action of acids. Subsequent researches have shown, however,
t the peculiar staining reactions are almost certainly due, not to any
perties of the surrounding membrane, but to peculiarities in the
cterial protoplasm itself. The researches of Hammerschlag have
own that a substance exists in the bacterial protoplasm which can be
lated and which has the staining peculiarities mentioned above. After
e removal of this substance the bacillus no longer retains its peculiar
staining properties, and it has also been shown that this peculiarity in staining is one more of mere difficulty in staining than of any peculiar reaction to acids or alkalies, for it has been shown that the bacillus tuberculosis can be stained by ordinary media without the addition of alkalies. The leprosy bacillus presents similar staining peculiarities, but it can also be easily stained by the method of Weigert, a property not possessed by the tubercle bacillus. The bacillus—or, more properly speaking, the group of bacilli—found in the smegma and also certain bacilli found in the cerumen take the same stain as the tubercle bacillus with ordinary methods. This peculiarity of staining is not, however, due to peculiarities in their protoplasm, but to the fact that they have grown in, and are surrounded by, substances containing large amounts of fat, which act as a protection against the acids used as decolorizing agents. Beinstock has shown that this peculiar reaction on the part of the smegna and cerumen bacilli can be entirely removed by submitting the cover-slip preparations under the action of heat to a solution of sodium in alcohol, by means of which the fatty capsule surrounding the bacilli is saponified, when the usual reaction no longer takes place.

For demonstrating the tubercle bacillus in sputum the following is the most satisfactory method: The sputum to be examined is spread out in a thin layer upon a glass plate which has been placed upon a dark or black background. The particles to be examined, which are the purulent specks, are picked out by means of a pair of sharp-pointed forceps, either with the naked eye or with the help of a pocket lens. The material thus obtained is carefully spread out upon the perfectly clean cover-slip and dried in the air, and then fixed by passing it slowly three or four times through the flame of a Bunsen burner. Special attention must be paid to the cleanliness of the cover-slip, as it has been shown that in cover-slips used for a second time, even after boiling, bacilli were still present from the first examination. The staining preparation best employed is that of Ziehl, which consists of—

Distilled water,	100 grammes;
Crystalline carbolic acid,	5 "
Alcohol,	10 "
Fuchsin,	1 gramme.

A few drops of the solution are placed upon the cover-glass, which is held over the flame until steam arises, actual boiling not being necessary. The glass is then washed in water, and a few drops of the Gabbet-Ernst solution are placed upon the glass and allowed to remain for about a minute. This solution consists of ¼ to ½ per cent. solution of methylene blue in 25 per cent. sulphuric acid. The cover-glass is then washed in water and mounted—if for temporary examination, in water; if for permanent keeping, in balsam. Tubercle bacilli are stained red, while the nuclei of the cells and other bacteria present are stained blue.

In the examination of urine or fæces the same process is carried through, the parts of material used being in urine the purulent sediment, and in the fæces the small particles of pus or muco-pus. When very small numbers of the tubercle bacilli are present, either in the sputum or in the urine, the centrifuge should be used.

The most satisfactory method for staining tubercle bacilli in sections is the following: The tissues are preferably hardened in absolute alcohol, though tissues hardened in Müller's fluid can be used after special preparation. The tissue is imbedded in celloidin, which is removed after the sections have been cut either with oil of cloves or with equal parts of absolute alcohol and ether. From these latter agents they may be placed in water. The dye to be used is that of Ziehl, the formula of which is given above. The sections are left for two hours at a temperature of 60° C., or for six to eight hours in the thermostat, or else for twenty-four hours at room temperature, the latter being perhaps preferable, as the heating is apt to cause shrinkage of the specimens. After staining by the fuchsin the tissues are decolorized in the ordinary acid alcohol of the laboratory, the 1 per cent. solution of hydrochloric acid in 70 per cent. alcohol. The tissues are removed from this decolorizing agent while they still retain a decided pink appearance, and are then placed in the counter-stain, a 2 per cent. aqueous solution of methylene blue. The sections are then dehydrated in absolute alcohol, cleared in oil of cloves, or preferably in xylol, and mounted in xylol balsam. By this method the tissues are stained a delicate blue and the bacilli a bright red color.

Methods of Growth of the Bacillus.—The tubercle bacillus does not grow upon the ordinary media found in the laboratory with the exception of potato, and on this the growth is not very satisfactory. Special media are necessary, the particular agent favoring the growth being glycerin. The difficulty of obtaining the original growth from tuberculous tissue is often great. This is partly due to the fact that the number of viable organisms in such material is, as a rule, small, and partly to the fact that, the growth of the bacillus being extremely slow, any contaminating organism introduced with the original material entirely overgrows the tubercle bacillus. After this primary difficulty has been overcome the growth of the organism becomes more and more satisfactory with each subsequent inoculation. The original growth is best obtained upon solid media, preferably glycerin agar or blood serum. On this medium at the end of ten days or two weeks, at a temperature of 37° to 38° C., there are observed small isolated colonies of a gray white color, having a dry, scaly, somewhat dull appearance. The best growth, however, of the organism is obtained in liquid media, a peptone illon containing a certain proportion of glycerin being the most sati- tory. A colony from a solid medium is allowed to float on the sur- of such liquid media, and in from ten days to two weeks a beauti- growth is usually apparent. This appears as a continuous thick te membrane, quite dry and wrinkled on the surface. Hardly any ner organism can be found which approaches the tubercle bacillus in intensity of growth on this medium.

Agents Deleterious to the Tubercle Bacillus.—The agencies which are pable of injuring the tubercle bacillus are of both physical and chem- l nature. The action of direct sunlight is perhaps the most effective the physical agents—so effective, indeed, that it is probable that all berculous sputum exposed in the open air is fully sterilized by the me that it has become desiccated and capable of transmission. The siccation of the organism has [illegible] less effect, and repeated experi- ments have shown that bacilli in desiccated sputum can retain their virulence for as long as nine or ten months (De Toma).

Heat acts upon the bacillus tuberculosis with comparative ease, and complete boiling for a very short time is all that is necessary to destroy the organism in fresh sputum or in foods containing it. Dry heat also has a rapid effect on the organism. Freezing does not destroy the bacillus.

Of the chemical agents, that which is most suited to disinfection of the bacillus is probably carbolic acid. The process of salting, by which material to be acted upon is exposed for long periods of time to solutions of chloride of sodium of a greater or less saturation, has been shown to have very little effect upon the virulence either of a pure culture of the bacillus tuberculosis (Galtier) or on meat from tuberculous animals (Forster). In connection with chemical agents it is well to mention the action of the gastric juice upon the tubercle bacillus, as it has been shown that whatever action this secretion has is entirely due to the hydrochloric acid which it contains, and not to its digestive power. The principal experiments concerning the action of the gastric juice upon the tubercle bacillus have been made by Falk and Wesener, and all tend to show that the bacillus is practically unaffected by the secretion, except after very long periods of exposure, such as could hardly obtain in the human body.

The Distribution of the Tubercle Bacillus in the Body.—The tubercle bacillus is found in the human body either in persons suffering from the various forms of tuberculosis or in normal individuals. It is to the work of Straus in particular that we owe our knowledge of the fact that the tubercle bacillus, like the diphtheria bacillus and certain other pathogenic organisms, is occasionally found in perfectly healthy individuals. His experiments show that it existed in a pure state in the nasal cavities of 9 out of 29 hospital attendants, in 1 out of 9 of the attendants upon public libraries, and in 1 out of 7 of those habitually employed in theatres. Other than in the nasal cavity no observations have been made upon the existence of the tubercle bacillus in normal individuals. In an individual suffering from tuberculosis the bacillus is invariably present in those lesions characteristic of the disease.

As a rule, the more acute the process the more numerous the tubercle bacilli, but in certain chronic processes occurring in the lung the number of bacilli is exceptionally large. The bacillus is also found in certain excreta from these individuals—notably in the sputum. As Nuttall has shown, from one and a half to four and a third billions of tubercle bacilli are daily thrown off by an individual with moderately advanced pulmonary tuberculosis. In the urine of those suffering from genito-urinary tuberculosis and in the stools of those suffering from intestinal tuberculosis the bacilli are also found, but usually in rather small numbers, especially in the stools.

Very few observations have been made upon the excretion of the tubercle bacilli in the milk of human beings (see p. 833), but there is abundant experimental evidence that bacilli may be excreted in large numbers in the milk of the lower animals, not only in those suffering from actual disease of the mammary gland, but in those in which such disease is not evident clinically.

The semen of individuals suffering from genito-urinary tuberculosis may contain large numbers of tubercle bacilli, and certain observers have claimed that in individuals suffering from tuberculosis in which the genito-urinary tract was free from gross lesions tubercle bacilli could also be obtained in the semen, but in very small numbers.

The sweat of tuberculous individuals has been shown to be free from the tubercle bacilli.

The Distribution of the Bacillus Outside the Body.—Although it has been shown that the bacillus tuberculosis is a strict parasite and can only multiply under parasitic conditions, there is abundant evidence that it can be present and in a virulent state outside of the human or animal body. Its presence under such conditions is very widespread, the number of bacilli depending largely upon the prevalence of tuberculosis in the affected district. It has been found in the dust of houses, streets, railroad cars, theatres, libraries, and various other public institutions. Outside of the dust, the only other source of contamination would appear to be in the food, either in the insufficiently cooked flesh of tuberculous animals or in the various products of such animals, as milk, butter, and cheese.

It has been shown that the tubercle bacillus can exist for a considerable length of time in water, but so far no authenticated instance of infection from this source has been reported. Since the work of Theobald Smith upon Texas fever in cattle we must admit the possibility of a conveyance of infectious diseases by insects, and, although no authenticated instance of this sort has been observed in tuberculosis, it has been shown that the common house-fly may harbor the tubercle bacilli.

(4) *Modes of Infection.*—(*a*) *Hereditary Transmission.*—The possibility of the direct transmission of tuberculosis has never been open to much doubt, but the method of transmission and the frequency are still under discussion. There are two opposing schools, the one claiming that the disease is transmitted by means of germ infection, the other claiming that the disease *per se* is not inherited, but only a tissue soil favoring its development.

The supporters of the former view, headed by P. Baumgarten, claim that in inherited tuberculosis actual tubercle bacilli have been carried over from the parent and lodged in the tissues of the child, where under suitable conditions they multiply and produce the disease. To

lain the late appearance in many instances after birth Baumgarten
his followers assume that the tubercle bacilli can lie latent in the
ues and subsequently develop when, for some reason or other, the
ividual resistance is lowered. He likens such cases of latent tuber-
osis to the late hereditary forms of syphilis, and explains the lack of
elopment of the germs by the greater resisting power of the tissues
children. This question of *latency* has recently been discussed fully
ore the Royal Medical and Chirurgical Society of London, and Kings-
n Fowler expressed the sensible opinion that it was not necessary seri-
usly to consider the question of latency in tuberculosis until direct
nsmission from mother to child was proved to be of frequent occur-
nce. Baumgarten bases his belief in germ transmission upon two
ain factors—the great frequency of the disease in early life and the
localization of tuberculous lesions in children.

In recent years statistics have shown the mortality from tuberculosis in the first years of life to be relatively high. Frœbelius in his analysis of 16,581 autopsies in sucklings found it is 416; some authors place the percentage much higher, Bolz, indeed, stating that in 2576 autopsies made on children 27.8 per cent. who died in the first year were tuberculous. The localization of tuberculous lesions in children in the bones or joints is very common, Cnopp's statistics showing that out of 298 tuberculous children of from a few days to twelve years of age, 147 had bone or joint tuberculosis, and only 8 of these showed evidence of visceral disease. Baumgarten is of the opinion that the accidental conveyance of tubercle bacilli to these points would not account for such a large proportion of cases, and expresses the view that the bacilli have been present since birth and have developed when favorable conditions are offered. The evidence in favor of Baumgarten's view is both clinical and experimental.

The clinical evidence exists in the form of undoubted cases of congenital tuberculosis, of which there are now, in man alone, some 15 or 20 examples in the literature;[1] besides these a number of spontaneous cases of congenital tuberculosis in the lower animals have been reported.

A number of laboratory workers have been able to show that congenital tuberculosis can be produced experimentally, the most prominent of these being Gärtner, who was able to cause tuberculosis in young mice by inoculating the mother with tuberculosis, either into the peritoneal cavity or into the blood stream.

The clinical evidence against Baumgarten's theory lies in the fact that the percentage of cases of congenital tuberculosis is extremely small. In the great majority of instances the organs of fœti born of tuberculous mothers give negative results when inoculated into guinea-pigs. Thus Vignal inoculated 24 guinea-pigs with the organs of 11 children born of tuberculous mothers with entirely negative results, and Bolognesi, who inoculated 130 animals either with the placentæ of 8 tuberculous women or with the organs of their offspring, only obtained two positive results in the animals.

The mass of the experimental evidence is against the theory of germ transmission. Gärtner, for example, who was able to show the possibility of germ infection, was only able, by inoculating into the peritoneal cavity, to cause 2 out of 9 canary birds to produce tuberculous eggs, and experiments by other observers all tend to show that the animals inheriting tuberculosis directly are in great minority.

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[1] For a review of the cases to date see Hahn in *Revue de la Tuberculose*, 1895, t. iii.

The possible methods of transmission of the germ in direct inheritance are three—transmission by the sperm; transmission by the ovum, and transmission through the blood by means of the placenta.

There is no clinical evidence to support the view that direct transmission can occur through the sperm, unless we consider the case of Sarney as such: a woman of thirty was delivered of a deformed fœtus in whose spinal column was a caseous focus containing tubercle bacilli. The woman was in perfect health, but her husband presented signs of tuberculosis. In order that the disease could be transmitted by the sperm it would be necessary that the tubercle bacilli should lodge in the individual spermatozoön which fecundated the ovum. The chances that such a thing could occur are extremely small, looking at the subject from a numerical point of view, although we know that tubercle bacilli do occasionally exist in the semen; they become still smaller when we consider that the spermatozoön is made up of nuclear material, which the tubercle bacillus is never known to attack. Experimentation is all opposed to sperm transmission, the work of Gärtner and others showing that the young of healthy female rabbits impregnated by tuberculous males are never tuberculous, even though the females themselves often contract the disease.

The possibility of transmission by the ovum must be accepted. Baumgarten has in one instance been able to detect the tubercle bacillus in the ovum of a female rabbit which he had artificially fecundated with tuberculous semen. The work of Pasteur on *pébrine* has shown the possibility of this form of transmission in the lower forms, though the question as to what effect such inoculation would have upon the human ovum cannot of course be answered.

Probably the almost constant method of transmission in congenital tuberculosis is through the blood current, the tubercle bacilli penetrating by way of the placenta. Certain authors hold that in these cases the placenta itself is invariably the seat of tuberculosis, and tubercles indeed have been demonstrated in several cases; but there are undoubted instances in which, with an apparently sound placenta, both the placental blood and the fœtal organs contained tubercle bacilli, notwithstanding the fact that the organs also appeared normal.

The opponents of the theory of germinal transmission hold that in cases of hereditary tuberculosis a special predisposition of the tissues exists toward the tubercle bacillus, though just what this predisposition is cannot be explained in our present state of knowledge. Perhaps the most important evidence in favor of this hereditary predisposition, and opposed to the theory of germ inheritance, is the fact that individuals of tuberculous stock will often pass through life without a sign of the disease when removed from sources of direct infection. Some instances reported by Bernheim are interesting in this connection. In one family which he mentions, consisting of five children born of a healthy mother to a tuberculous father, one child was taken from home soon after birth and brought up by a relative. The rest of the children continued living with their parents. The child who was removed from home remained and strong, while, of the other four, two died of pulmonary tuberis and two were in advanced stages of the same disease. In r family of seven children, in which both father and mother were ulous, the second and fifth children had never lived with the . The children who lived with their parents died of tuberculosis; her two remained healthy and had healthy children of their own. e whole question of heredity in tuberculosis can be summed up in e statements: that though cases of congenital tuberculosis occur, are extremely rare; that in all probability most cases of heredituberculosis are due to heredity of the soil, and not to inheritance e germ; that tuberculosis is much more frequently transmitted in maternal than in the paternal line.

No circumstance, perhaps, has contributed more to the belief in the reditary transmission of the disease than the frequency with which erculosis is met with in the ascendants of those affected. The estites range from 10 per cent. to 25 per cent., or even in some instances 50 per cent. Some of the statistics on this point are worth quoting: n 1000 cases Williams found 48.4 per cent. with family predisposition, 12 per cent. with parental, 1 per cent. with grandparental, and 34.4 per cent. with collateral heredity. Of 250 cases in which Solly made very careful inquiries on this point, there were 28.8 per cent. with parental, 7.6 per cent. with grandparental, and 19.2 per cent. with a history of collateral heredity. Of 427 cases at the Johns Hopkins Hospital, there were 53 in which the mother had had tuberculosis, 52 in which the father had been affected, and 105 in which a brother or sister had had the disease.

As illustrated in the instances mentioned by Bernheim, the question of family infection is the all-important one, and Hilton Fagge very wisely remarks that it is impossible to draw a line between hereditary and accidental tuberculosis, as naturally the children of an affected parent are more liable to accidental contamination.

(*b*) *Inoculation.*—Only tuberculous matter when inoculated produces tuberculosis. It was the great merit of Villemin to demonstrate in 1865 the infective nature of the disease. In man transmission by inoculation, which is rare, is chiefly met with in persons whose occupation brings them in contact with dead bodies or with animal products. Demonstrators of morbid anatomy, butchers, and tanners are liable to a local tubercle of the skin, particularly of the hands, which forms a reddened mass of granulation tissue. This has long been known as the post-mortem wart—the *verruca necrogenica* of Wilks. The tuberculous nature of this body is shown by the existence of bacilli and by inoculation experiments in animals. It forms one of the most interesting examples of a local tuberculous process, which may exist for years without showing any tendency to spread. It should in reality be classified with lupus, with which in general and histological character it appears to be identical. These tubercles may persist for years without any change. Of many scores which in former years I have had on my hands, only one lasted for more than a twelvemonth. They show no tendency to spread, though occasionally smaller ones—colonies—may start up in the neighborhood. Mr. Hutchinson refers to a case in which the anatomical tubercle had persisted for more than forty years. I have never known an instance of infection of the lymph glands, though the possibility of this is shown by a case by Gerber, who accidentally inoculated his hand in performing a post-mortem in a case of phthisis, which was followed by a "lichen" tubercle, which, after persisting for months, was excised. Shortly after this the lymph glands of the axilla, having become enlarged and painful, were removed, and characteristic tuberculous changes with bacilli were found in them. I have seen it stated that possibly Laennec contracted phthisis from this source, but this seems very improbable, as he did not die until twenty years after the inoculation, and in the interval had no manifestations pointing to this as the source of the disease.

In the performance of the rite of circumcision tuberculosis has not infrequently been inoculated, the infection being due to disease in the operator and occurring in connection with the habit of cleansing the wound by suction.

In various other ways the disease has been inoculated. Local tubercle of the ear has resulted from perforation of the lobe for earrings. The bite of a tuberculous patient has been followed by local disease, or inoculation has occurred from a cut by a broken spit-glass of a consumptive patient, and instances of infection have followed transplantation of skin (Czerny). There is no evidence that tuberculosis has ever been transmitted in the operation of vaccination. On the other hand, it has been shown that the lymph from the vesicles of revaccinated consumptives is non-infective. The possibility of it, however, cannot be denied.

(*c*) *Infection by Inhalation.*—A belief in the contagiousness of pulmonary tuberculosis has always been held in the profession. The early Greek physicians referred to it, and in the Latin races it seems always to have prevailed. Among the English-speaking races until recently very little credence was given to this view. Morton in the *Phthisiologia* recognized it, and refers to a young man who married a phthisical girl and became affected *ex contagio*.

It is well remarked by Cornet, "The consumptive in himself is almost harmless, and only becomes harmful through bad habits." It has been fully shown that the expired air of consumptives is not infective. The virus is only contained in the sputum, which when dry is widely disseminated in the form of dust, and constitutes the great medium for the transmission of the disease. "In order to be air-borne the sputum must be dried and broken up into dust. If discharged into a handkerchief, it speedily dries, especially if it is put into the pocket or beneath the pillow. In the last stages of consumption the patient becomes weak, the sputum is expelled imperfectly, pillows, sheets, handkerchiefs are soiled. If a male, the beard or moustache is smeared. Even in the hands of the cleanly, without special precautions, such circumstances all tend to the production around the patient of a halo of infected dust maintained by every process of bedmaking or of cleaning which includes the pernicious process happily described as 'dusting.' In the hands of the careless and the dirty the infectivity is, of course, greatly aggravated. It attains its maximum of intensity where the filthy habit of spitting on the floor prevails, especially if it is carpeted" (James B. Russell).

Cornet has shown that the dust of rooms, hospital wards, and other calities frequented by patients with pulmonary tuberculosis contains e bacilli and is infective. The observations of Straus show how these cilli may be found in the air-passages of perfectly healthy individuals. tached to particles of dust, the bacilli gain entrance to the system rough the lungs, which may be regarded as the great portal of inva- The extraordinary frequency with which local disease occurs in e organs and in the bronchial glands will be referred to later. A siderable number of persons dying by accident or disease show that one time or another the bacilli have effected a lodgement in these rts. Even when the bronchial glands exhibit no signs of tuberculosis e bacilli may be present and prove infective (H. P. Loomis).

In institutions, such as jails, barracks, and convents, and particularly in those in which the occupants are greatly restricted in the important element of fresh air, tuberculosis is specially prevalent. In a review of thirty-eight cloisters, embracing the average number of 4028 residents, among 2099 deaths in the course of twenty-five years 1320 (62.88 per cent.) were from tuberculosis. In some cloisters more than three fourths of the deaths are from this disease, and the mortality in all the residents, up to the fortieth year, is greatly above the average, the increase being due entirely to the prevalence of tuberculosis. It has been stated that nurses are not more prone to the disease than other individuals, but Cornet says that of 100 nurses deceased, 63 died of tuberculosis. The more perfect the prophylaxis and hygienic arrangements of an asylum or institution the lower the mortality from tuberculosis. In the Alabama Insane Hospital, during a period of three years and nine months, of 295 deaths, 28 per cent. among the whites and 42 per cent. among the negroes were caused by tuberculosis (Bondurant). The mortality in prisons has been shown by Baer to be four times as great as outside. The death rate from phthisis is estimated at 15 per cent. of the total mortality, while in prisons it constitutes from 40 to 50 per cent., and in some countries, as Austria, over 60 per cent. In institutions of this sort, in addition to the presence of the bacilli, the lowered vitality, and in prisons the mental depression, must lower the resistance. In a single ward in the city of Philadelphia Flick studied the distribution of the deaths from tuberculosis for a period of twenty-five years. He found that not less than one third of the houses of the ward became infected during this period, and more than one half of all the deaths from this disease during the year 1888 occurred in these infected houses.

In hospitals and sanitaria the number of nurses and attendants who are attacked is in indirect ratio to the stringency with which proper sanitary precautions are carried out. It is stated that in the Paris hospitals the attendants are decimated by tuberculosis. At the Brompton Consumption Hospital in London the doctors, nurses, and attendants are very rarely attacked. With ordinary care there is no reason that consumptives should infect the wards which they occupy. At the Adirondack Sanitarium, I. H. Hance has recently examined the dust of the buildings, some of which have been inhabited by consumptives for a period of ten years. Sixteen out of seventeen buildings were free from infectious material. The infected cottage was one always occupied by two patients in an advanced stage, one of whom had complained that his room-mate had been spitting about carelessly.

The frequency of marital infection indicates the special danger when the contact is very intimate. Of the replies to a collective investigation on the question of contagion in tuberculosis (Committee of the British Medical Association), there were 261 in the affirmative, of which 158 were supposed to be due to infection through marriage. Several of Weber's cases are of special interest. One patient lost four wives in succession, one lost three, and four lost two each. Of 427 cases of pulmonary tuberculosis at the Johns Hopkins Hospital, in 25 either husband or wife was affected with or had died of tuberculosis.

(*d*) *Infection by Milk.*—The prevalence of intestinal and mesenteric tuberculosis in children suggests that the food supply may be the source of infection. It has been shown experimentally that the disease may be transmitted to young animals fed with the milk of tuberculous cows. It is stated also that butter made from such milk may prove infective. The pigs of a tuberculous sow have been found with intestinal tuberculosis of the most advanced grade. The experiments of Gerlach, Bang, Bollinger, and Ernst have proved how readily the disease may be transmitted. Ernst states that the bacilli may be present and the milk be infective even when there is no tuberculous mammitis; but in the work of the Royal Commission on Tuberculosis, Martin could not induce the disease artificially in animals inoculated or fed with the milk of tuberculous cows whose udders were healthy. On the other hand, he states that "the milk of cows with tuberculosis of the udder possesses a virulence which can only be described as extraordinary; all the animals inoculated showed tuberculosis in its most rapid form." The practice of drinking cow's milk raw and of feeding the same to children is not without danger. When there is the slightest doubt as to the source the milk should be boiled.

(*e*) *Infection by Meat.*—This mode perhaps plays a very minor rôle in the etiology of human tuberculosis. It has been shown that the meat of tuberculous animals is not necessarily infective. Martin suggests that it may acquire this property by accidental contamination with tuberculous matter during its removal. The ordinary process of cooking destroys the virus. With reference to the confiscation of the carcasses of tuberculous animals, the Royal Commission concludes: "Provided every part that is the seat of tuberculous matter be avoided and destroyed, and provided care be taken to save from contamination by such matter the actual meat substance of a tuberculous animal, a great deal of meat from animals affected by tuberculosis may be eaten without risk to the consumer." It would be safer, however, to confiscate the flesh of all tuberculous animals, the State providing proper compensation.

(5) *Conditions Influencing Infection.*—(*a*) *General.*—Environment is an all-important predisposing factor. Dwellers in cities are much more prone to the disease than residents of the country. Not only is the liability to infection very much greater, but the conditions of life are such that the powers of resistance are apt to be weakened. As already stated, sunlight is one of the most powerful agents in destroying the tubercle bacillus, so that in imperfectly ventilated dwellings and workshops, and in residences in close, dark alleys, and in tenement houses the liability to infection is very much increased. The influence of environment was never better demonstrated than in the

own experiment of Trudeau, who found that rabbits inocu-
with tuberculosis if confined in a dark, damp place without sun-
and fresh air rapidly succumbed, while others treated in the same
but allowed to run wild, either recovered or showed very slight
s. The occupants of prisons, asylums, and poorhouses, too often,
l, in barracks and large workshops, are in the position of Trudeau's
s in the cellar, and under conditions most favorable to foster the
pment of the bacilli which may have lodged in their tissues. The
nt respiration of air already breathed, upon which MacCormac
lfast laid so much stress, appears to render the lungs less capable
isting infection.

Soil and locality are believed by many to have a very important
ring on the development of tuberculosis. The observations of
ry I. Bowditch in this count Buchanan in England show
the disease prevails more w in the wet, ill-drained districts—
increase which is associated wi ghtened vulnerability and greater
bility to catarrhal affections of an ds. The influence of the dwelling
has been already referred to in connection with Flick's work. No
ngle condition is of greater importance than that which relates to the
proper arrangement and ventilation of the dwelling-houses. Here in
parallel columns is the contrast drawn by Dr. Thorne Thorne between
dwelling which will tend to promote and a dwelling which will tend
to prevent consumption:

"*Conditions of Dwelling-house tending to the Promotion of Tuberculous Consumption.*	"*Conditions of Dwelling-house tending to the Prevention of Tuberculous Consumption.*
"1. A soil either (*a*) naturally damp and cold, or (*b*) subject to the influence of the rise and fall of a subsoil water lying within a few feet of the surface.	"1. A soil which is dry (*a*) naturally, or (*b*) freed by artificial means from the injurious influence of dampness and of the oscillations of the underlying subsoil water.
"2. A dwelling-house of which either the foundations, the area they enclose, or the walls are, by reason of faulty construction or otherwise, liable to dampness.	"2. A dwelling-house so constructed as to be protected against dampness of site, foundations, and walls.
"3. Such immediate surroundings of the dwelling-house as tend to prevent the free movement of air about it and its ample exposure to the influence of sunlight.	"3. Such open space on at least two opposite sides of the dwelling-house as shall secure ample movement of air about it, together with its free exposure to the influence of sunlight.
"4. Such structural defects as would prevent the maintenance within all parts of the dwelling-house of ample movement of air by day and night, and free exposure of its habitable rooms to daylight."	"4. Such construction of the dwelling-house as will secure for its habitable rooms and throughout its interior free movement of air by day and by night and the free access of daylight."

(*b*) *Individual Predisposition.*—The fathers of medicine, more particularly Hippocrates, Aretæus, and Galen, laid great stress upon the bodily conformation of those prone to consumption. A great deal was written on the so-called *habitus phthisicus*, which Hippocrates described in the following terms: "The form of body peculiar to subjects of phthisical complaints was the smooth, the whitish, that resembling the lentil; the reddish, the blue-eyed, the leuco-phlegmatic; and that with the scapulæ having the appearance of wings." Undoubtedly the long, narrow, flat chest with depressed sternum is commonly enough seen in tuberculous patients, but there are only too many individuals with perfectly well-shaped chests who fall victims annually to the disease. The tuberculous or scrofulous diathesis, upon which formerly so much stress was laid, is now regarded simply as an indication of a type of conformation in which the tissues are more vulnerable and less capable of resisting infection. Beneke's investigations on the viscera of phthisical patients indicate that the heart is relatively small, the arteries proportionately narrow, and the pulmonary artery relatively wider than the aorta. He suggests that this may lead to increase in the intrapulmonary blood pressure, and so favor catarrhal processes. The lung volume he found relatively greater in those affected with tuberculosis. A study of the composite portraiture of pulmonary tuberculosis has been made by Galton and Mahomed. In 442 patients they separated two types of face—one ovoid and narrow, the other broad and coarse featured. This corresponds in an interesting way to the diathetic states formerly recognized—namely, the tuberculous, with thin skin, bright eyes, oval face, and long, thin bones; and the scrofulous, with thick lips and nose, opaque skin, large, thick bones, and heavy figure. These conditions, on which so such stress was formerly laid, indicate, as Fagge states, nothing more than delicacy of constitution, incomplete growth, and imperfect development.

(*c*) *Influence of Age.*—No age is exempt. The disease is met with in the suckling and in the octogenarian. Pulmonary tuberculosis occurs most frequently, as stated by Hippocrates, from the eighteenth to the thirty-fifth year. From the fifth to the tenth year individuals are less prone to the disease. At different ages different organs are more prone to be involved. During the first decade the bones, meninges, and lymph glands are more frequently affected than at subsequent periods.

(*d*) *Sex.*—The influence of sex is very slight. Women are perhaps somewhat more frequently attacked than men, due, possibly, to the fact that in a more sedentary, in-door life they are more liable to infection. Pregnancy and lactation also are two conditions which are apt to lower, perhaps, the resistance of the organism.

(*e*) *Race.*—The negro, who it is stated is not specially prone to the disease in Africa, is in America and in the West Indies very subject to tuberculosis. The relative immunity of the Jews has been mentioned (page 730).

(*f*) *Occupation* is an important predisposing factor. The inhalation of impure air in occupations associated with a very dusty atmosphere renders the lungs less capable of resisting infection. The incidence of pulmonary tuberculosis among the workers in mills and factories is very high, and in certain occupations, such as glass-workers, stone-cutters, and coal-miners, and the whole group of trades which lead to pneumonokoniosis, favors the development of tuberculosis.

(*g*) Certain *local conditions* influence infection, among which the following are the most important:

Catarrhal Bronchitis. The influence of catarrh of the respiratory passages in pulmonary tuberculosis is well recognized. How often is a neglected cold blamed as the starting point of the disease! It seems to by lowering the resistance and favoring the conditions which enable he bacilli either to enter the system or, when once in it, to develop. The liability of lymphatic tuberculosis in children is probably associated with the common catarrhal processes in the tonsils, throat, and bronchi.

Certain of the specific fevers predispose to tuberculosis, among which easles and whooping cough stand pre-eminent. They are often associated with a bronchial catarrh. In some of the cases it is probably not a fresh infection which follows, but the blazing of a smouldering fire. Typhoid fever is thought by some to predispose to tuberculosis, but my experience is opposed to this view. Of other affections, influenza, vari-la, and syphilis are all believed to favor the development of the disease. Diabetes, as is well known, very often terminates in pulmonary tuberculosis, particularly in young persons.

Chronic heart disease, arterio-sclerosis, aneurysm of the aorta, forms of chronic nephritis, cirrhosis of the liver, and the various forms of cerebro-spinal sclerosis, all are conditions which favor infection. It is remarkable in how many of the subjects of these disorders in general hospital practice the fatal event is a terminal acute tuberculosis, most frequently of the serous membranes. Subjects of congenital or acquired contraction of the orifice of the pulmonary artery usually die of tuberculosis. On the other hand, mitral valve disease, particularly stenosis, is stated to antagonize the disease (J. E. Graham). In children catarrhal entero-colitis probably favors the development of tabes mesenterica.

The influence of hæmoptysis and pleurisy will be referred to later.

Trauma. Surgeons have laid great stress upon this as an etiological factor in tuberculous processes. Experiments indicate that tissues which have been bruised, and which would in health have readily and rapidly destroyed organisms, promote their growth under the altered conditions. Probably in the case of tuberculosis following trauma the injured part is for a time a *locus minoris resistentiæ*, and if bacilli are present they may by it receive a stimulus to growth or under the altered conditions be capable of multiplying. Not only in arthritis, but in pulmonary tuberculosis, traumatism may play a part. The question has been thoroughly studied by Mendelssohn, who reports nine cases in which, without fracture of the rib or laceration of the lung, tuberculosis developed shortly after contusion of the chest. Operation upon tuberculous lesions may be followed by a general infection. Resection of a strumous joint is occasionally followed by acute tuberculosis. Of 837 resections, 225 ended fatally, 26 with acute tuberculosis (Wartmann).[1]

THE GENERAL MORBID ANATOMY AND HISTOLOGY OF TUBERCLE.

(1) *The Distribution of Tubercles in the Body.*—The distribution of tubercles in the organs and tissues of the body varies greatly according to the primary seat of the disease and according to certain peculiarities of individual organs and tissues; the bacilli may find their way into the circulation either by the blood or lymph channels, and lead to the formation of scattered foci of tubercles which are found in the internal

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[1] A recent study of the question is to be found in vol. ii. of *Revue de la Tuberculose*, by Depage and Gallet.

organs. In cases of general tuberculosis, where the bacilli are carried into the blood in large numbers, the tubercle nodules are evenly distributed throughout the organs, though to macroscopical investigation they seem to be much more numerous in one organ than in another. Miliary tubercles in the liver are often very difficult to distinguish macroscopically, whilst, on the other hand, those in the spleen and kidney are usually easily made out. On microscopical examination, however, the liver, which to the naked eye has seemed to contain but few tubercles, is often found studded with them. The great difficulty in making out tubercles in certain organs, particularly in the pancreas and thyroid gland, has led to the belief that these organs are relatively immune to the attacks of the bacillus. This belief, as Chiari pointed out, is false, microscopical examination showing in most cases of miliary tuberculosis numbers of tubercles in both the organs mentioned. Certain of the organs and tissues of the body, however, do seem to be almost immune against tuberculosis, particularly the œsophagus, the inner lining of the larger arteries, and the voluntary muscles. The fact that the latter are resistant is often strikingly illustrated in cases in which both layers of the pleura are infiltrated by the tuberculous process, which, however, stops sharply at the subjacent intercostal muscles. The one organ which is almost always affected in tuberculosis, as seen at the autopsy table, is the lung, and this is true both of children and adults. Here may be mentioned the very frequent occurrence of healed lung tuberculosis in all classes of cases, the healed area generally appearing in the form either of an area of dense fibrous material or of an encapsulated caseous or calcareous nodule. Apart from the lung, the organs are affected with tubercle with varying frequency at varying periods of life; in children the lymph glands, bones, and joints are attacked most frequently.

(2) *Changes Produced by the Tubercle Bacilli.—The Nodular Tubercle.*—The most distinctive lesion produced by the bacillus tuberculosis is the nodular tubercle, accurate descriptions of the histology of which we owe particularly to the painstaking researches of Baumgarten. The fact must never be lost sight of that in their early stages tubercles do not present any peculiarity in their histological components or arrangement. Similar aggregations of cells may be caused by foreign bodies, certain animal parasites, and the dead products of the tubercle bacilli, and in certain stages the so-called lymphomata of the liver, occurring in typhoid fever, are strikingly like young tubercles. The evolution of the tubercle following the introduction of the tubercle bacillus into the tissues may be traced as follows:

(*a*) *The Multiplication of the Tubercle Bacilli.*—This begins almost immediately after the introduction of the organism. The growth is quite rapid, and is accompanied by its dissemination into the surrounding tissues, partly by direct growth, and partly by mechanical dissemination in the lymph stream. The action of phagocytes in connection with the dissemination of the bacilli has not been accepted by most pathologists, and probably does not occur. From an early date many of the bacilli are found in the fixed tissue cells of the affected tissue.

(*b*) *The Multiplication of the Fixed Cells.*—From the fifth day after the introduction of the tubercle bacillus into the tissue changes can be

e out indicative of multiplication of the fixed cells by the indirect
thod of subdivision, as evidenced by the abundance of karyokinetic
res to be found in the affected region. This cellular subdivision
ts not only the fixed connective tissue cells of the part, and the
thelial cells, and the lining of the smaller bloodvessels, but the
of the parenchyma of the affected tissue can also be seen to be in
state of active subdivision. As a result we have the production of
unded or irregularly cuboidal cells with vesicular nuclei, which re-
able epithelial cells, and are hence called epithelioid cells. Almost
m the first appearance of these cells tubercle bacilli can be demon-
ated in the interior of a certain number of them. In some only a
gle bacillus can be made out; in others the cell is closely packed with
mass of bacilli, often having the appearance of a typical "leprosy cell."

(c) *The Invasion by Leucocyte*.— llowing the formation of the epi-
thelioid cells other cells are soon to be made out in the tubercle which
re evidently of vascular origin, as they show no signs of multiplication,
he only changes they undergo being of a regressive character. These emigrant cells are of two varieties—the polynuclear leucocyte, and the small mononuclear element of the blood, the so-called lymphocyte. The polynuclear leucocytes appear much more susceptible to injury than the mononuclear variety, and undergo regressive changes with great rapidity. The mononuclear variety, on the other hand, are much more slowly destroyed, and as the tubercle increases in size the leucocytes represented are in large part these small round elements which are situated particularly at the periphery of the nodule.

(d) *The Formation of a Reticulum.*—About the tenth or eleventh day a fine network is to be seen between the cells composing the tubercle—a network first pointed out by Wagner, and which is best demonstrated in specimens hardened in osmic acid. This reticulum is composed, according to some pathologists, of the pre-existing connective tissue elements which have undergone a rarefaction from the pressure of the growing tubercle cells. It exists particularly at the periphery of the tubercle, and the fibres composing it can at times be made out to be directly continuous with the fibres of the surrounding connective tissue. The recent researches of Falk would tend to show that there is also present in the tubercle nodule from an early stage—that is to say, before the existence of degenerative changes—definite fibrillary fibrin, also most abundant at the periphery of the tubercle, and undergoing destruction in the subsequent degenerative processes through which the tubercle passes.

(e) *The Formation of Giant Cells.*—In the large majority of tubercles there are present, besides the varieties of cells above mentioned, large cells containing from four or five to twenty-five or thirty nuclei—so called giant cells. These are formed either from the fusion of individual cells or much more probably from the indefinite multiplication of the nuclei in a single cell, the protoplasm failing to divide with the nuclei. The character of the nuclei in these cells is the same as that of the epithelioid cells composing the tubercle, and the great mass of evidence goes to show that the giant cells are epithelioid cells whose nuclei have subdivided indefinitely, whilst their protoplasm has lost its power of subdivision, probably on account of the injurious influence exerted upon it by certain products of the tubercle bacillus. The giant cell is generally irregularly round or oval in shape. It varies in diameter from two to three mikrons, and often shows at various points on its periphery distinct branching prolongations. The giant cell is not by any means characteristic of tuberculosis, but the type of giant cell associated with this disease—Langhans' giant cell—is so characteristic and so seldom found in other conditions that it has been called by certain German writers the finger-post of tuberculosis. The chief characteristic of the tuberculous giant cell which distinguishes it from most other forms is the peculiar arrangement of its nuclei, either around the periphery of the cell or at one or both of the poles. This is due to the fact that the centre of the giant cell, like the centre of the tubercle, in the mid-portion of which it generally lies, is particularly prone to undergo degenerative changes, so that whilst at an early stage in its development nuclei exist throughout the protoplasm of the giant cell, those in the centre of the cell are soon destroyed, the remaining one having a mural or polar arrangement according as the cell is round or oval.

(3) *The Degeneration of Tubercle.*—The ultimate fate of all tubercles is degeneration. This is not due, as was formerly supposed, to lack of nutrition, for much larger areas than those represented by a tubercle may be nourished without a direct blood supply. The agents which lead to the degeneration of the tubercle are the tubercle bacilli themselves and their products. In order to produce this degeneration the living bacilli themselves are not necessary, the researches of Prudden, and later of Kostenitsch, having shown that the dead bacilli and the bacterial products are capable of setting up exactly similar changes. The forms of degeneration which the tubercle may undergo are two—caseous and fibrous.

(*a*) *Caseous Degeneration* (*Caseation*).—This form of degeneration, which is the most common, may occur at any stage in the process of tubercle formation. It is often seen in the very earliest stages, and in its most characteristic form is seen in tuberculous glandular masses and in certain forms of lung tuberculosis. Weigert pointed out that the process was one of coagulation necrosis. The cells in the centre of the tubercle die slowly, and are transformed into coagulated homogeneous or finely granular masses, showing absence of nuclear staining or at most but fine nuclear fragments taking the stain. These masses subsequently undergo fatty infiltration and take on a white, opaque appearance resembling cheese; hence the name caseation. In the miliary tubercle these caseous masses are seen as the opaque yellow centre of the nodule, the gray, translucent periphery representing the non-degenerated portion of the tubercle. The aggregation of many caseous tubercles leads to the formation of the much larger masses so commonly seen in the more chronic forms of the disease. At the beginning of the process the tubercle bacilli can still be demonstrated with good staining reactions in the degenerated mass. At a later date many or even all the bacilli may lose their staining power, though this apparently harmless material is still capable of setting up the disease when inoculated into susceptible animals. In some instances, as in certain forms of lung tuberculosis, the caseous material everywhere contains large numbers of tubercle bacilli. The cheesy masses may undergo secondary changes, some of which are favorable, others unfavorable, to the progress of the disease. In some instances they soften and break down into a rather thick, grumous fluid, forming the so-called tuberculous abscess. The contents of such abscesses do not, however, consist of true pus, but mainly of broken-down cellular products, often showing an extreme grade of fatty change. Another form of softening with true pus formation is seen where the caseous focus becomes secondarily infected with pus organisms. Here, besides the detritus above mentioned, we have all the constituents of true pus. A more conservative process may often take place in the caseous material, leading to the production of a dense fibrous capsule about the mass—so-called encapsulation. In these instances the fluid element of the caseous material may be almost entirely absorbed, leaving the encapsulated substance as a dry and friable, but still somewhat cheesy-looking, material. In some other instances a deposit of lime salts takes place in the caseous area, which here, again, may become surrounded by a fibrous capsule and remain innocuous in the tissues for years.

(*b*) *Sclerosis.*—In many cases, particularly in individuals who possess good powers of resistance, a more conservative process occurs in the tubercle—the so-called sclerosis or fibroid change. This is seen most frequently in the lungs and in the peritoneal cavity, and is the method by which the spontaneous cure of tuberculous lesions takes place. The process consists in the formation, sometimes with, sometimes without, caseation, of fibrous tissue, with the disappearance of the tubercle as such, the final result being its transformation into a small nodule of dense fibrous tissue. In the case of the already cheesy tubercle the fibroid process takes place from the cellular part of the nodule surrounding the caseous centre, the new cells originating from the pre-existing tubercle cells. Where the process tends to be fibroid from the beginning the whole tubercle may lose its cellular structure at an early period and become transformed into a small fibrous tumor mass.

(4) *The Diffused Infiltration Tubercle.*—In many parts of the body, more particularly in the lungs, the tuberculous process, except in very acute cases, does not manifest itself as discrete nodules, but as a more or less extensive diffuse process, which results from the fusion of many small tuberculous areas. As a matter of fact the small nodule which we are accustomed to regard as the ultimate tubercle—the miliary tubercle—is, as has been pointed out by Virchow, in many instances not single, but a mass of very small tubercles, the true ultimate tubercle being submiliary in size and on the limit of visibility so far as the naked eye is concerned. As seen in the lung the areas of infiltrated tubercle present to the naked eye a grayish, translucent appearance, and often particularly in the later stages, a caseous centre. These areas vary greatly in extent, some occupying only a few lobules, and again a whole lobe, or even a whole lung, being affected. In many instances the course of the smaller bronchi is beautifully mapped out by the process, which occurs as a series of peribronchial tuberculous masses. At times a whole lobe is consolidated, giving rise, after caseation has taken place, to the appearance designated as caseous pneumonia—a condition previously regarded as being due to the superaddition of the tuberculous infection upon a preceding croupous pneumonia, but which we now know to be entirely due to the action of the tubercle bacillus. The

whole process, from the formation of the miliary tubercle to the complete consolidation of a large lobe of the lung, can be followed out step by step with suitable preparations.

(5) *Secondary Inflammatory Processes in Tuberculosis.*—The formation of tubercles, particularly in the lung, is associated with the production of secondary inflammatory processes of a non-specific character. These are not due, as a rule, to the action of the tubercle bacillus itself, but to certain irritative products which it produces and which find their way into the surrounding tissue. The irritation thus caused leads in the lung to the formation of areas of catarrhal pneumonia immediately about the tubercle, the exudate consisting of but a small amount of fibrin, and, as a rule, but few polynuclear leucocytes, the chief element being desquamated and proliferated epithelial cells originating from the lining membrane of the alveoli. Associated with this exudation is an inflammatory condition of the alveolar walls, with proliferation of the connective tissue elements—a process which varies according to the acuteness of the case, and which in the more chronic forms of the disease may lead to the production of large amounts of fibrous tissue which shut off the tuberculous process and limit, to a great degree, its tendency to spread. Whether the tubercle bacillus can induce actual suppuration is still much discussed. That it is usually not a pus-producer in the strict sense is no doubt correct, the so-called tuberculous pus consisting of caseous material and cellular débris. There seems to be no doubt, however, that the tubercle bacillus can in some instances be a true pus-producer, and occasionally cases are seen which show true pus in the histological sense and in which this organism is alone concerned.

II. ACUTE TUBERCULOSIS.

Acute Miliary Tuberculosis.

In this form the bacilli are distributed throughout the body by the blood, and the clinical picture is that of an acute infection. The anatomical lesions are widely distributed throughout the organs in the form of miliary granulations, which are found upon the serous membranes, in the lungs, liver, lymph glands, kidneys, spleen, in the endocardium, in the membranes of the brain, in the bone marrow, and occasionally in the choroid coat of the eyes. Their distribution is unequal. They may be abundant in some organs and scanty in others. The meninges of the brain may be densely packed with tubercles, while there are but few in the abdominal and thoracic viscera. On the other hand, the lungs may be stuffed with granulations out of all proportion to those in other organs. The appearance and structure of the miliary granulations has already been described. Etiologically, two forms are distinguished, the primary and the secondary.

The existence of a primary miliary tuberculosis rests upon the occurrence of cases in which, after the most scrupulous and thorough examination of all parts, no focus of tuberculous disease has been found. In such cases it has been assumed that the blood infection has been ct, though it is difficult to see how it could take place. On the er hand, it is to be remembered how difficult it is to positively lude the presence of a primary caseous focus in the body.

In an immense majority of all the cases the disease is secondary, and an auto-infection arising from a pre-existing tuberculous focus, often ent and unsuspected. Among the common sources of the general fection are local tuberculous disease of the lungs and of the bronchial nds—the latter particularly in children—tuberculosis of the bones d of the kidneys or of the testes, and less frequently tuberculosis of e skin. Sometimes acute miliary tuberculosis has followed operative ocedures upon tuberculous foci. By far the most common sources of fection are small foci of disease in the lungs and caseous masses in the racheal and bronchial glands. The infection results, as a rule, from the direct invasion of a vein by the tubercle, or the rupture of a softened nodule or of a caseous bronchial gland into one of the pulmonary veins. The observations of Weigert have shown how frequent is this invasion of the walls of the veins in the neighborhood of tuberculous masses. In other cases the general infection may result from invasion of the lymphatics, and there are many instances now on record in which the general infection has resulted from invasion of the thoracic duct. Doubtless it depends greatly upon the number of bacilli which enter the circulation whether a general infection results. A small number may be distributed without doing any harm.

It is often impossible to say what has determined the sudden and violent onset of the disease. It would seem, indeed, as though special conditions favored the production of a local or a general miliary tuberculosis. Thus after certain fevers, particularly measles and whooping cough in children, the disease is by no means uncommon, and in adults the weakness and debility following protracted fevers seem predisposing factors. In Bright's disease, chronic cardio-vascular affections, and cirrhosis of the liver the patients are very frequently carried off by terminal miliary tuberculosis.

SYMPTOMS.—For practical purposes we may divide the cases into those in which the manifestations are general, and those in which they are local, predominating in certain organs, as the lungs, meninges, pleuræ, or peritoneum.

1. *General or Typhoid Form.*—The picture is that of an infectious disease with few if any local symptoms, the course and general features of which may very closely resemble typhoid fever. The patient generally has shown signs of failing health with loss of appetite for a week or two. There may have been headache, chilly feelings, slight cough, and digestive disturbances. Even epistaxis has been noted in some cases, so that the period of invasion may simulate closely that of typhoid fever. Then the patient becomes feverish, the tongue is dry, the pulse rapid, the respirations increase, and there is often cough. The early bronchitis may still further complicate the picture. The pulse is seldom dicrotic. The temperature does not show the steady ascent of typhoid fever. From the outset it is more irregular and the remissions are greater. Sometimes, indeed, the pyrexia is intermittent, and in the early morning hours the temperature may be normal or subnormal. In a few cases there has been observed an inverse type in which the tem-

perature is highest in the morning. In very rare instances there may be little or no fever, particularly toward the close. From Bäumler's clinic Reinhold has called particular attention to these afebrile forms of acute tuberculosis. In 9 out of 52 cases there was either no fever or only a transient rise. As mentioned, the delirium is usually early, and there may be great restlessness and jactitation. Photophobia may be a marked feature. Nervous twitchings and subsultus are frequent symptoms. Cutaneous hyperæsthesia is a prominent feature in some cases. The respirations are usually increased, particularly in the early stage; there are signs of diffuse bronchitis and a slight cyanosis is common. The cheeks are usually flushed. Cheyne-Stokes breathing may develop toward the close. As the disease progresses there is much torpor and dulness, which often deepens toward the close into coma.

Albuminuria is almost constant, and the diazo reaction is frequently observed in the urine.

Gastric symptoms are common. There may be early anorexia. Vomiting is not infrequent, and diarrhœa may occur, and even hemorrhage if there are tuberculous ulcers in the bowels. The abdomen may be slightly distended and the spleen can usually be felt.

The differential diagnosis between this form of miliary tuberculosis and typhoid fever may be very difficult. If seen at the onset, the irregularity of the temperature curve in the former is a point of great importance. In tuberculosis the respirations are usually more frequent and the tendency to slight cyanosis more marked. Diarrhœa is rare in tuberculosis, but there are instances in which the diagnosis has been still further complicated by the occurrence of blood in the stools. The enlargement of the spleen in general tuberculosis is neither so early nor so marked as in typhoid fever, except perhaps in children. The presence of the diazo reaction may increase the confusion. The absence of the characteristic rash of typhoid fever is a very important feature. Occasionally in acute tuberculosis reddish spots may develop on the skin, but they do not come out in crops, and they rarely have the characters of a true typhoid eruption. Toward the close petechiæ may appear.

The examination of the blood may give important information. In a few instances tubercle bacilli have been demonstrated. The absence of a leucocytosis is in favor of typhoid fever. It is only in the very acute cases of tuberculosis without any suppurating foci that the leucocytosis is absent. The eyes should be carefully examined for choroidal tubercles. In protracted cases cultures should be made from the stools and urine by Elsner's method in order to determine the presence or absence of the bacillus typhi.

2. *Local Forms.*—(*a*) *Pulmonary.*—The patient may have had cough for months or years without special impairment of health, or he may have been the subject of chronic pulmonary tuberculosis. In other cases, more particularly in children, the affection is met with as a sequence of measles and whooping cough or may follow influenza. From the very outset the pulmonary symptoms are marked. There is a diffuse bronchitis, with shortness of breath, cough, and the expectoration of mucopurulent, occasionally rusty, sputa. Hæmoptysis has been noted in a few cases. From the start dyspnœa is a special feature, and may be out of all proportion to the intensity of the physical signs. The cheeks are

usually suffused and the lips and nose and finger tips a little cyanotic. With the exception of emphysema and the later stages of severe pneumonia there is no other pulmonary condition in which the cyanosis is so pronounced a feature. The physical signs are those of bronchitis. In children there may be defective resonance at the bases from scattered areas of broncho-pneumonia, or, what is equally suggestive, areas of hyper-resonance. Indeed, the percussion note, particularly in the front of the chest in some cases of miliary tuberculosis, is full and clear, and it will be noted (post-mortem) that the lungs are unusually voluminous. This is the result of a more or less widespread acute emphysema. On auscultation the râles are either sibilant and sonorous or small, fine, and crepitant. There may be fine crepitation from the occurrence of tubercles on the pleura (Jürgensen). In children there may be high pitched tubular breathing at the bases or toward the root of the lung. Toward the close the râles may be larger and more mucous. The temperature rises to 102° or 103° F., and may present the inverse type. The pulse is rapid and feeble. In the very acute cases the spleen is always enlarged. The disease may prove fatal in ten or twelve days or may be protracted for weeks or even months.

The DIAGNOSIS of this form is less difficult, and is consequently more frequently made, than in the general or typhoid form. The history of previous cough, the existence of tuberculous foci elsewhere, or the onset of the disease in children after measles are among the suggestive features. The sputa may contain tubercle bacilli. In a few cases choroidal tubercles may be found.

(*b*) *Acute Tuberculous Pleurisy.*—This will be considered in Tuberculosis of the Serous Membranes (page 766).

(*c*) *Acute Tuberculous Peritonitis.*—This will be considered in the same section (page 770).

In a few instances acute miliary tuberculosis involves both pleura and peritoneum simultaneously. There are cases also in which with the onset of the disease the synovial membranes have been involved, so that the disease has been regarded as acute rheumatism.

(*d*) *Meningeal Tuberculosis; Acute Tuberculous Meningitis; Acute Hydrocephalus; "Water on the Brain."*—Our first accurate knowledge of this affection dates from the publication of Robert Whytt's *Observations on the Dropsy of the Brain*, Edinburgh, 1768. The literature is very fully given in the last edition of Barthez and Sannee.[1]

Though Guersant had as early as 1827 used the name *granular meningitis* for this form of inflammation of the meninges, it was not until 1830 that Papavoine demonstrated the nature of the granules and noted their occurrence with tubercles in other parts.

In 1832 and 1833, W. W. Gerhard[2] of Philadelphia made a very careful study of the disease in the Children's Hospital at Paris, and his publications, more than those of any other author, served to place the disease on a firm anatomical and clinical basis.[3]

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[1] *Maladies des Enfants*, 1891.

[2] *American Journal of the Medical Sciences*, vols. xiii., xiv., and xvii.

[3] The description which he gives of the 10 cases observed by him at the Children's Hospital, Paris, between Aug. 1, 1832, and Aug. 1, 1833, is a model clinical study which should be carefully read by those interested in the subject.

MENINGEAL TUBERCULOSIS.

ETIOLOGY.—This is by far the most important of all the acute meningeal affections. It is very much more common in children than in adults. While rare during the first year of life, it is most common between the second and the fifth years. It is, however, by no means an uncommon disease in adults. Between the years 1884 and 1889 in the canton of Zurich 569 persons died of tuberculous meningitis—275 males and 294 females. Of these, 454 were under fifteen years of age, and 115 from the fifteenth to the seventieth year (Kraemer).

In a few instances the disease attacks individuals in perfect health and living under the most favorable conditions. In a majority of cases, however, there are predisposing factors—previous ill health or a prolonged illness, in children particularly the fevers. Other instances follow overstrain at school or prolonged mental excitement. The hereditary influence has probably been exaggerated. Cases are more common in neuropathic families, and a special predisposition cannot be denied, as there have been families in which a number of children have been successively attacked.

The disease is rarely primary. In an immense proportion of all cases tuberculous disease exists in other organs. Cases are reported in which, after the most thorough inspection of the entire body, tubercles have been found only in the meninges, but it is very difficult to exclude the presence of foci in the bones or in the bone marrow. It has been suggested that the bacilli may reach the meniges through the cribriform plate of the ethmoid bone, and Demmé has recorded a case of probable infection from tuberculous rhinitis. In this connection we may refer again to the demonstration by Straus of the presence of tubercle bacilli in the nostrils of healthy persons. By far the most common source of infection is the lungs, either a local lesion which has become latent or a progressive caseous broncho-pneumonia. Lesions of the lymph glands come next in order, particularly those of the bronchi and of the mesentery. In other cases the disease follows tuberculous lesions of the bones or joints, pleurisy, the cold tuberculous abscess, or uro-genital tuberculosis. The infection may be through the lymph channels, but in the majority of cases is through the bloodvessels, and in this connection it is interesting to note that as early as 1878 Huguenin concluded that the disease originated, as a rule, from embolism.

PATHOLOGICAL ANATOMY.—On removing the calvarium and the dura mater the pia mater is usually reddened, its vessels engorged, the convolutions of the brain are flattened and the sulci somewhat obliterated. It is rare to see exudate in any amount on the cortex. The meninges at the base are most involved, hence the term basilar meningitis. The parts about the optic chiasm, the Sylvian fissures, and the interpeduncular space are affected. There may be only slight turbidity and matting of the membranes, and a certain stickiness with serous infiltration; but more commonly there is a turbid exudate, fibrino-purulent in character, which covers the structures at the base, surrounds the nerves, extends out in the Sylvian fissures, and appears on the lateral, rarely on the upper, surfaces of the hemispheres. The tubercles may be very apparent, particularly in the Sylvian fissures, appearing as small whitish nodules on the mem-

nes. They vary much in number and size and may be difficult to
l. The amount of exudate bears no definite relation to the abundance
tubercles. The arteries of the anterior and posterior perforated
s should be carefully withdrawn and searched, as upon them
lar tubercles may be found when not present elsewhere. In doubt-
cases the middle cerebral arteries should be very carefully removed,
ad on a glass plate with a black background, and examined with a
objective. The tubercles are then seen as nodular enlargements on
smaller arteries. The lateral ventricles are dilated (acute hydro-
nalus) and contain a turbid fluid; the ependyma may be softened,
l the septum lucidum and fornix are usually broken down.

The minute anatomical changes have been very thoroughly studied by many observers. In a recei per Hektoen[1] has studied the subject with great care, and draws the owing conclusions:

1. "In tuberculous meningitis there is a tuberculous endarteritis characterized by the formation of intimal tubercles and a diffuse subendothelial, intimal proliferation due to implantation of tubercle bacilli from the blood. From the endarteritis the infiltration may spread into the muscular coat and the adventitia, and the whole wall may undergo caseous and hyaline degeneration.

2. "Tuberculous proliferation in the adventitia may invade the media and the intima, and the whole wall of the arterial segment may undergo degeneration.

3. "The veins are constantly the seat of more or less extensive infiltration, which always results from adjacent extravascular or arterial foci.

4. "The epithelioid cells of the subendothelial, tuberculous intimal proliferation are most likely derived from the subendothelial layer of connective tissue, and not from the endothelial lining."

In a much larger proportion of cases than has been supposed the spinal meninges are also involved, and there are cases in which the symptoms are chiefly spinal. In rare instances the spinal meninges may be involved alone. In the case of a sailor who was admitted to the Montreal General Hospital, who three weeks before his death had fallen on the deck, the symptoms were chiefly spinal, and were very naturally attributed to the trauma. The post-mortem showed an extensive eruption of miliary tubercles with much turbid fibrinous exudate over the entire spinal pia mater. There was neither exudate nor tubercles present in the basilar meninges. There were small cheesy masses at the apices of the lungs.

SYMPTOMS.—The features of onset are very variable. In a few instances the disease sets in abruptly with symptoms of the most intense cerebral excitement or mania, and proves rapidly fatal within a few days. In this, the so-called apoplectic form, the cerebral cortex is specially involved. In the large proportion of all cases the disease runs a more subacute course, while in adults the disease may be prolonged over a period of months.

The course of the disease has been divided into three or four stages, which are sometimes clearly marked, but which are often not well defined. A prodromal stage, a period of excitation, and a period of paralysis are recognized by most writers. While in a few cases the onset is abrupt, with active and maniacal delirium, as a rule there is a longer or shorter period of failing health. Sometimes the symptoms set in after one of the eruptive fevers or they follow a fall. The child becomes irritable and restless and at night sleeps badly, and there is loss of appetite, and also a change in the disposition. Headache, tired feelings, or actual pains in the limbs may occur. There may be obstinate vomiting and nausea, and constipation. In young children the onset may be with a convulsion. There is rarely fever in this prodromal stage.

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[1] *Journal of Experimental Medicine*, vol. i. No. 1.

The onset is characterized by aggravation of the headache, vomiting, constipation, and fever. The pain in the head is often intense and agonizing. The face is usually flushed, and at intervals when the pain becomes very intense the child utters a short, sudden cry—the so-called hydrocephalic cry. The headache is most commonly frontal, but in many instances it is general. It is much exaggerated by noise, by light, and by any movement. The child may sometimes scream continuously with the pain in the head until quite exhausted. The screaming may lead to error in diagnosis. I remember a young girl aged thirteen whom I saw in West Philadelphia, who for three days, except when under the influence of strong sedatives or chloroform, screamed incessantly and loudly, so that she could be heard for the distance of a square away. At first we suspected hysteria, but with the onset of fever she became quieter and gradually developed the symptoms of a well marked basilar meningitis.

Vomiting is a very common symptom and is independent of the taking of food. It usually stops in a day or two, but there are cases in which it persists throughout the course. Constipation is the rule, often of a most obstinate character, resisting purgatives of great potency. The fever, from the onset of which we may count the commencement of the disease, is at first moderate, rarely reaching above 102° F., and presenting an evening exacerbation. A very high temperature at the onset is rare. The pulse is at first rapid, ranging in an infant from 130 to 160. The tongue is usually furred, the breath often offensive. The abdomen in this stage may be prominent. As the disease advances the child does not like to be disturbed; the face has a dull, fixed aspect; the light is irritating, and on attempting to move or examine the child it resists and cries. There may be delirium. The pupils at this stage are often contracted, and transient strabismus may be noted. The reflexes are usually exaggerated, and there may be marked cutaneous hyperæsthesia. A not uncommon feature is a blotchy erythema, and there is often marked vasomotor disturbance. If the finger nail is drawn across the skin of any region, a red line comes out quickly—the so-called *tâche cérébrale*. Important symptoms of this period are disturbances of motility. In the period of excitation there may be recurring general convulsions, which sometimes in adults resemble those of epilepsy. Local convulsive movements are common, and may be unilateral, of the arm, face, and leg muscles, or the cortical irritation may be limited to certain motor areas. In some instances prolonged tonic spasms may occur. When of the neck and back muscles, there is retraction of the head, and when the spinal meninges are involved as well, there may be opisthotonos. This period of excitation and irritation persists for a week or ten days. There may be then a very deceptive remission in the general symptoms; the fever may lessen, and the child may look brighter and regain consciousness.

In the final period, or stage of paralysis, the fever is higher, the convulsive movements become perhaps exaggerated, and there is a deepening of the coma, so that the child cannot be roused. Spasmodic contractions are frequent and the retraction of the head persists. There may be much tremor and twitching of the tendons, and local paralyses occur. Ptosis and strabismus are common; the pupils are usually dilated. The respirations are often much disturbed, either sighing or there is well marked Cheyne-Stokes breathing. The pulse becomes more rapid and irregular. The temperature often sinks, and may become subnormal. There may be an ante-mortem elevation of temperature, the fever rising to 105° or 106°, or even extreme hyperpyrexia, 110° F. The sphincters are relaxed and there is incontinence of urine and fæces; diarrhœa usually occurs. The pulse becomes very rapid; the skin is bathed in perspiration; the extremities become cold, and tracheal râles announce the fatal event.

The ocular features of the disease require special mention. In the early stages the pupils are usually contracted; at the middle period of the disease they may be unequal, and, as a rule, with increase in the intracranial pressure they become dilated and immobile. There may be conjugate deviation of the head and eyes. The third nerve is most frequently involved, causing ptosis or strabismus. An exudate at the inferior and internal part of one crus may cause the syndrome of Weber—paralysis of the third nerve on one side, with paralysis of the face, limbs, and hypoglossal nerve on the opposite side. Of the deeper changes in the eye, optic neuritis is the most important; the process, however, is rarely of great intensity. Tubercles of the choroid are much less frequently seen during life than post-mortem figures would indicate. Litten found them at autopsy in 39 of 52 cases. They were present in only 1 of 26 cases examined by Garlick; 41 cases were examined with negative results by Heinzel.

The duration of the disease is variable. Very acute cases may prove fatal within a day or two. It is stated that Wunderlich saw a fatal result within thirty hours. A majority of the cases last about three weeks, while there are others, particularly in adults, which drag on for ten, twelve, or even sixteen weeks. Some of these more chronic cases display the symptoms of a cortical meningitis, sometimes with pronounced psychical symptoms or those of cerebral tumor.

Certain special forms of tuberculous meningitis deserve brief mention. In a few instances the disease develops in the newborn or within the first months of life. The symptoms are often obscure; the course of the disease is very brief, and death may follow within a few days in convulsions.

Tuberculous meningitis of adults is seen most commonly in individuals who present well marked features of disease in other parts, most commonly in the lungs. There may be headache, increase in the fever, or the onset may be characterized by a furious delirium. Convulsions are by no means uncommon, and they may be localized. Well marked Jacksonian fits may recur for weeks. Remarkable amelioration of the general symptoms of tuberculosis may occur. In other instances there are tetanic spasms or persistent rigidity of an extremity.

DIAGNOSIS.—The diagnosis of tuberculous meningitis is, as a rule, easy in children. The vague and uncertain features of the prodromal stage may sometimes awaken one's suspicions, particularly in a family in which tuberculosis has prevailed. The symptoms of onset—headache, fever, and vomiting—are common enough in many disorders of childhood, particularly in the initial stage of the fevers. A day or two usually suffices to clear up the diagnosis.

There are three conditions, however, which demand special notice: First, the symptoms associated with otitis media in children. On several occasions I have seen cases in which headache, vomiting, and fever were most suggestive of oncoming meningitis, and in which the whole trouble was due to middle-ear disease. In an instance which I saw recently the child had made little or no complaint of the pain in the ear, and it was not till the third or fourth day, after presenting symptoms of great severity, that a discharge took place from the right ear, with prompt relief.

Second, the cerebral symptoms which are associated with gastroenteritis in children. There may be convulsions, coma, squint, and contracted pupils, with irregularity of the pulse and Cheyne-Stokes respirations. The condition has been called false hydrocephalus, or, as Marshall Hall termed it, the "hydrencephaloid" state. The child is in a semicomatose condition, with the eyes open and the fontanelles depressed.

A third important condition is associated with pneumonia, more frequently in children than in adults. The cerebral symptoms may be the more marked from the onset, and not a single feature of the early stages of meningitis may be lacking—the vomiting, constipation, intense headache, photophobia, and even the cry. The local pulmonary symptoms may be completely obscured or overlooked. Very often, too, in these cases the pneumonia is of the apex, and there may be little or no expectoration. I have known cases in which there was not a suspicion entertained of the existence of pneumonia; but the autopsy showed the meninges to be perfectly free from exudate and a localized consolidation of the apex or of a lower lobe.

In a few instances, too, children who are teething or who have a transient dyspepsia present for a day or two cerebral symptoms which may suggest meningitis.

Typhoid fever may simulate closely tuberculous meningitis. On several occasions I have performed autopsies on supposed meningitis and found the meninges free from all inflammation, while the intestines showed the lesions of typhoid fever. It is well to remember Stokes' dictum, that in the fevers "there is no single nervous symptom which may not and does not occur independently of any appreciable lesion of the brain, nerves, or spinal cord."

The differential diagnosis between the tuberculous and the simple forms of meningitis is not always possible. The history of a previous tuberculous lesion or the presence of some focus of disease or caseous glands, the recent recovery from one of the fevers, the more insidious onset, the protracted course, and the symptoms pointing specially to involvement of the base are all points which favor the diagnosis of tuberculous meningitis.

Prognosis.—Tuberculous meningitis is almost invariably fatal Instances of recovery are on record, but there is always in these a doubt as to the diagnosis. I have not seen an instance of recovery in a case which I regarded as tuberculous. The possibility, however, cannot be denied. Wallis Ord and Waterhouse have reported a case of recovery in a child of five years after trephining and drainage. A recovery has followed Quincke's lumbar puncture.

III. TUBERCULOSIS OF THE LYMPHATIC SYSTEM.

I. Tuberculosis of the Lymph Glands (Scrofula).

The very word scrofula has almost disappeared from our vocabularies. In a recently issued voluminous work on Pediatrics the name does not occur in the index. This remarkable change has followed the demonstration of the tuberculous nature of scrofulous lesions. Formerly special attention was given to different types of scrofula, of which two important forms were recognized—the sanguine, in which the child was slightly built, tall, with small limbs, a fine clear skin, soft silky hair, and was mentally very bright and intelligent; and the phlegmatic type, in which the child was short and thick-set, with coarse features, muddy complexion, and a dull, heavy aspect.

Tuberculous adenitis occurs at all ages, and, though more common in children than in adults, it is not at all infrequent in the middle periods of life, and may be met with in extreme old age. So far as I know, there is no instance on record of congenital tuberculous adenitis. Practically, in all cases the disease follows infection from without, and it is specially prevalent in the three great groups of glands which stand at the gateways of the lymphatic system—namely, the cervical, the tracheo-bronchial, and the mesenteric. While it is doubtless possible for tubercle bacilli to pass through a normal mucous membrane, yet recurring catarrhal inflammation, by rendering the passage more easy and by exciting slight adenitis of the neighboring glands, is probably a special predisposing factor. In a child with a constantly recurring nasopharyngeal catarrh the bacilli find the gateways less strictly guarded, and are taken up by the lymphatics and passed to the nearest glands. The importance of the tonsils as an infection atrium will be referred to later, as local disease of these glands seems not uncommon. In conditions of health the local resistance—or, as some would put it, the phagocytes—would be active enough to deal with the invaders, but the irritation of a chronic catarrh weakens the resistance, and the bacilli are enabled to develop and gradually to change a simple into a tuberculous adenitis. The frequent association of tuberculous adenitis of the bronchial glands with whooping cough and with measles, and the development of tubercle in the mesenteric glands in children with intestinal catarrh, find in this way a rational explanation. After all, as Virchow pointed out, an increased vulnerability of the tissue, however brought about, is the most important factor of the disease.

Certain general features of tuberculous adenitis may be first referred to:

The local character of the disease. In a great majority of all cases the cervical lymph glands are alone involved, perhaps on only one side. The bronchial lymph glands are very often found affected without any evidence of other tuberculous lesions in the body, and one or two of the mesenteric glands may be found cheesy.

Tuberculous adenitis tends to heal spontaneously in a very considerable proportion of all cases. Nowhere are healed tuberculous lesions more common than in the bronchial and mesenteric lymph glands.

The cheesy masses in tuberculous adenitis frequently break down into puslike liquid, which is usually sterile. This softening—or suppuration, as it is often called (though true pus may not be present)—is often the result of a mixed infection.

The existence of an unhealed focus of tuberculous adenitis is a constant menace. One can safely say that in more than three fourths of all cases of acute tuberculosis the infection has been derived from cheesy lymph glands. It has been urged by Marfan that scrofula in childhood affords a sort of protection against tuberculosis in adult life, but the evidence of this is by no means satisfactory.

CLINICAL FORMS.—(1) *Generalized Tuberculous Lymphadenitis.*—There are cases in which the lymphatic system is alone affected, and the glands, internal and external, with or without the serous surfaces, present advanced tuberculosis without much involvement of the viscera. This is a more common type of the disease than is usually supposed, and occurs both in children and in adults. In the former there are cases in which the lymph glands are progressively involved, usually beginning in the groin and then attacking those of the axilla, and lastly the cervical and internal groups. Lesage and Paschal, who have described a number of cases, believe that the affection is due in some to cutaneous tuberculosis, but in others they think it may be congenital.

The symptoms are those of a progressive cachexia without much fever and without signs of disease of the lungs or of the abdominal organs. In children such cases must be carefully distinguished from the general slight enlargement of the glands in syphilis, and from the moderate enlargement of the superficial lymph glands which may follow the infectious fevers. In adults a tuberculous polyadenitis is not so common, but there are cases in which the bronchial, retroperitoneal, and mesenteric glands are greatly enlarged and caseous, usually with involvement of the cervical groups; there may be high and irregular fever, and the patient may die without involvement of any of the viscera. In the acute form some of these cases resemble very closely Hodgkin's disease, as in a patient in the Montreal General Hospital in whom this disease was diagnosed, and whose enormously enlarged cervical and axillary glands were found post-mortem to be tuberculous.

(2) *Local Tuberculous Adenitis.*—(*a*) *Cervical Group.*—The drainage area of the lymph glands of the neck includes the superficial and deep structures of the head and neck. The most important groups are the superficial cervical beneath the platysma, which drains the side of the head and neck and face and external ear, and the deep cervical group along the carotid sheath, which drains the mouth, the tonsils, the palate,

pharynx, and larynx. The submaxillary and suprahyoid groups drain the lower gums, the front of the mouth and tongue, the chin, and lower lip.

Tuberculous adenitis of the glands of the neck is by far the most common form. Fortunately, it often remains local, and formerly was regarded as the most typical and characteristic manifestation of scrofula. It is very prevalent among the children of the poor and in those who live in the crowded, unhealthy dwellings in large cities. Children in foundling hospitals and asylums are also specially subject to it. In this country it is very prevalent among the children of the negro race. In the widespread prevalence of tubercle bacilli in the dust of cities and in institutions any of us may inhale or swallow the germs. The habits of children render them very much more liable than others to become infected. As already mentioned, the bacilli can probably pass through healthy mucosa. The slight catarrhal troubles of the naso-pharynx which are so common in children probably open the portals and allow the bacilli to reach the lymph glands. Preliminary irritation and enlargement of the glands in connection with eczema of the scalp or ear or with conjunctivitis or keratitis weaken, no doubt, the powers of resistance. The glands may enlarge rapidly at first, and become soft and painful. The swelling may, however, be gradual and painless from the outset. The enlarged "kernels," as they are popularly called, are usually more prominent on one side than on the other. As they increase the individual tumors can be felt, separate, smooth, and firm. Often a chain of glands can be felt from the angle of the jaw to the clavicle. As they enlarge they form knotted masses in which the outlines of the individual tumors can be just felt. The skin is, as a rule, freely movable, but as areas of softening occur it becomes adherent and reddened, and finally ulcerates, discharging a cheesy matter and a thin, watery pus. The opening thus formed has very little tendency to heal, and the skin about it is livid and undermined. Many of the glands may suppurate in this way, and when healing ultimately takes place the sides of the neck are disfigured by irregular, unsightly scars. When the glands are large and growing actively there is fever, and the patients are usually anæmic. Death rarely follows, and a considerable proportion of all cases get quite well. In other instances the axillary glands are involved, and there is a continuous chain extending beneath the clavicle and the pectoral muscles. In many of these cases the tracheal and bronchial glands are also attacked, and there is a special liability to involvement of the pleura; and in young adults tuberculosis of the cervical lymph glands is not infrequently followed by involvement of the apex of one lung.

(*b*) *Tracheo-bronchial Group.*—The lymph glands within the thorax are of the greatest importance in connection with tuberculosis. The sternal are placed along the course of the internal mammary vessels; the intercostal, along the heads of the ribs and sometimes extending outward; the anterior mediastinal group, between the lower part of the sternum and the pericardium; the cardiac group, in the interpleural space about the arch of the aorta; and, lastly, the tracheal glands, on either side of the windpipe, and the bronchial proper, continuous with them, which surround the main bronchi and pass deeply in the roots of the lungs. There are also glands in the posterior mediastinum along the thoracic aorta and œsophagus. Tuberculosis of these groups is extraordinarily common, and in a very large proportion of all cases in children the first infection is in them. Of 125 cases of tuberculosis examined by Northrup in children, the bronchial glands were involved in every instance, and in 13 of these cases the disease was limited to these glands alone. The observations of H. P. Loomis show that even in apparently normal glands tubercle bacilli may be present and the tissue prove infective to animals.

The anatomical condition of the glands varies greatly. There may be gray miliary nodules or large cheesy areas with foci of softening, or the glands may be hard, deeply pigmented, and calcified. The tracheal group may be affected without great involvement of the bronchial glands. In some instances the substernal glands are found much more enlarged than those about the bronchi. In children the greatly enlarged caseous glands often pass deeply into the hilus of a lung, and in some instances, destroying the capsule of the gland, merge directly with areas of caseation in the lung tissue itself. When the glands suppurate the abscesses may perforate in different directions. The effects of these enlarged glands are very varied, and for full details the reader is referred to the elaborate section in the *Traité* of Barthez and Sannée (tome iii). It is sufficient here to say that there are instances on record of compression of the superior cava, of the pulmonary artery, and of the azygos vein. The trachea and bronchi, though often flattened, are rarely seriously compressed. The pneumogastric nerve may be involved, particularly the recurrent laryngeal branch. More important, really, are the perforations of the enlarged and softened glands into the bronchi or trachea, or a sort of secondary cyst may be formed between the lung and the trachea. Perforations of the vessels are much less common, but the pulmonary artery has been opened. Perforation of the œsophagus has been described in several cases. One of the most serious effects is infection of the lung or pleura by the caseous glands situated deep along the bronchi. This may, as is often clearly seen, be by direct contact, and it may be difficult to determine in some sections where the caseous bronchial gland terminates and the pulmonary tissue begins. In other instances it takes place along the root of the lung and is subpleural. Among other sequences may be mentioned diverticula of the œsophagus following adhesion of an enlarged gland and its subsequent retraction, and, in the case of the anterior mediastinal and aortic groups, the frequent production of pericarditis, either by contact or by rupture of a softened gland into the sac.

Authors differ widely in their views as to the symptoms caused by enlarged glands along the bronchi and trachea. Certainly in a great many cases the manifestations are quite trivial. How often does one find enormous enlargement of these glands in a child who has presented no symptom whatever pointing to disturbance of the organs within the chest! Among the symptoms Barthez and Sannée speak of compression of the veins, leading to dropsy; of dilatation of the veins, causing cyanosis; of alterations in the character of the heart sounds; and of attacks of paroxysmal dyspnœa, crouplike in character, with cyanosis. By some these paroxysms have been ascribed to compression of the vagi, and not to direct pressure on the bifurcation of the trachea. A bronchus may be compressed by the enlarged and caseous glands, and cause feeble breathing in one lung, with sibilant râles.

In the diagnosis of enlarged mediastinal glands some writers have laid great stress upon the information obtained by percussion, particularly the dulness on the upper part of the sternum and in the interscapular spaces.

(c) *Mesenteric and Retroperitoneal Groups.*—Tuberculous affection of the glands of the mesentery, of the retroperitoneum, and of the gastro-hepatic omentum is extremely common, particularly in children. Of 127 cases of fatal tuberculosis in children noted by Woodhead, these structures were involved in 100, while Ashby states that of 103 consecutive post-mortem examinations on children dying of tuberculosis, in 62 there was tuberculous ulceration of the intestines; in 71 there were cheesy mesenteric glands; in 55, both ulcers and cheesy glands; in 7, tuberculous ulcers without involvement of the glands; and in 16, cheesy glands without ulcers. Of 144 children in whom the mesenteric glands were tuberculous, only 44 showed neither ulcerations nor tubercles in the intestines (Barthez and Sannée). In a large number of the cases the infection is primary in these glands; a lesion of the mucosa of the bowels is not necessary. In children it is highly probable that many cases are due directly to infection with tuberculous milk.

The symptoms of "abdominal scrofula," as it was called by the older writers, are very varied. Slight tuberculous affection of a few glands is met with commonly enough in children who have died of various disorders. These groups may be involved in tuberculous polyadenitis, particularly with the general lymphatic tuberculosis already referred to. The most important condition is that to which the term *tabes mesenterica* is usually applied. The cases are seen chiefly in children between the ages of eighteen months and five years who have had chronic intestinal catarrh. The diarrhœa is the most troublesome symptom. The stools are frequent, yellow brown in color, and contain mucus, but not often blood. The abdomen is distended, a little painful on deep pressure, but no nodules are felt. There is usually slight fever, but the general wasting and debility are the most characteristic features. The disease is chronic, extends over a year or two, and leads to the most extreme emaciation. It is sometimes not at all easy to determine whether there is actual tuberculous disease of the bowel or not, as a chronic intestinal catarrh may be associated with a similar condition of extreme debility and wasting.

In other instances of tabes mesenterica the peritoneum is involved and nodular masses may be felt, and the abdominal distention may be still greater.

In a few cases the tuberculous mesenteric glands form large abdominal tumors.

II. TUBERCULOSIS OF THE SEROUS MEMBRANES.

(1) **Tuberculosis of the Pleura.**—The relationship of acute pleurisy to tuberculosis has been the subject of much discussion. While the views on the subject are varied, the general trend of opinion has been

strongly in favor of the closeness of the association. Landouzy and his pupils believe that nearly all cases of pleurisy are tuberculous in origin. Pleurisy *á frigore* is held to be of very rare occurrence, and the great majority are held to be an expression of an incipient pulmonary tuberculosis which may appear at any subsequent time, even after the lapse of years. Fiedler states that of 112 pleurisies that were aspirated, 21 recovered, 25 died of phthisis, and the 66 which recovered from the pleurisy were found to be the victims of other tuberculous diseases. Vincent Y. Bowditch in looking up the subsequent history of 90 cases of pleurisy which occurred in his father's practice found that 32 had either died of tuberculosis or had developed some definite tuberculous disease. Sears collected from the literature records of 451 cases of pleurisy, of which 176, or about 39 per cent., had either died of pulmonary tuberculosis or had become the subject of some tuberculous affection. There are others, particularly Blachez, Vidal, Dreyfus-Brisac, who think that the tendency to regard the great majority of cases of pleurisy as tuberculous in origin or as precursors of later tuberculous disease has been exaggerated. Statistics of writers who hold the latter opinion would seem to show that persons who have been the subject of pleurisy do not develop tuberculosis subsequently any oftener than those who have not had an attack. The balance of opinion, however, favors a more or less intimate relationship between the two diseases. In the study of the cases in the Johns Hopkins Hospital which I made for the Shattuck Lecture (1893) I found that the incidence of tuberculous pleurisy in post-mortem examinations on individuals who had been the subjects of pleuritic effusion—either fibrinous, sero-fibrinous, hemorrhagic, or purulent—was a trifle less than 32 per cent. The pleurisy was tuberculous in 32 instances out of 101 successive cases in which effusion was present.

Although, clinically, there is nothing positively characteristic of tuberculous pleurisy, there are features, to say the least, suggestive. A slow, insidious onset is common, although by no means distinctive. Indeed, the disease may come on abruptly with a stitch in the side or even with a chill. The order of frequency of the commonest symptoms of which the patients complain, and for which they seek relief, are cough, dyspnœa, pain in the side, and lastly chills and fever. Cough and loss of weight for several months, hæmoptysis, or a previous attack of pleurisy are significant points in the patient's history. There may be tuberculosis in the family, although in many cases no such positive information is obtainable. The character and contents of the exudate vary greatly. It may be sero-fibrinous, simply serous, hemorrhagic, sero-purulent, or purulent. Of these the hemorrhagic and sero-purulent are the most frequent. The thin, slightly opalescent, sero-purulent exudate, often with a greenish tint, and which microscopically contains granular, fatty matter and only a few leucocytes, is almost characteristic of a tuberculous lesion. The cover-slip and culture tests give variable results. It is generally conceded by bacteriologists that the great majority of tuberculous effusions are sterile; organisms are neither found on the cover-slip preparations nor is any growth obtained on culture media. A sterile effusion is therefore regarded as favoring the tuberculous character of a pleurisy. In one of my cases with sero-fibrinous exudate tubercle bacilli were definitely determined in the effusion after the patient had been tapped on repeated occasions. The bacteriological examination of the purulent tuberculous exudates also gives variable results. In a certain percentage of acute cases tubercle bacilli may be abundant. They may occur alone, as was demonstrated by Prudden in one of his cases. In other instances only pus organisms or diplococci are present, or the exudate may be entirely negative. Pansini has emphasized the importance, from a technical standpoint, of examining larger quantities of exudate than can be obtained by the usual exploratory puncture with the hypodermic syringe and the use of animal inoculations, as without such precautions the bacilli may readily escape observation. His own studies, made on large quantities of the exudate, showed tubercle bacilli present in 6 instances out of 15 cases of sero-fibrinous effusion. The importance of the injection of the exudate into the peritoneal cavity of guinea-pigs has been demonstrated by French observers, who have obtained positive results in the sero-fibrinous and purulent pleurisies of individuals apparently not tuberculous.

The nature of a pleurisy may not be apparent for months or years, when the onset of tuberculosis in other parts may indicate the true character of the process. From year to year I am more and more impressed with the frequency with which the subjects of pleurisy with effusion subsequently develop tuberculosis.

Tuberculous pleurisy may be a part of a general miliary infection, but rarely do the pleuritic symptoms dominate, or even become pronounced enough to attract attention. From the character of the onset and the course of the disease one recognizes two main classes—acute, and the subacute and chronic tuberculous pleurisies, to which may be added a third, the pleurisy which forms a part of a general serous membrane tuberculosis.

1. ACUTE TUBERCULOUS PLEURISY.—As already stated, it is impossible to estimate the proportion of instances of acute pleurisy due to tuberculosis, which has been variously placed at from 40 to 80 per cent. of all cases. The disease is rarely fatal during the acute attack. Many cases entirely recover, a few become chronic in their course, and a variable number develop tuberculosis at some later date. We are able to recognize three groups of cases in which the onset is acute:

(*a*) *Acute Tuberculous Pleurisy with Subsequent Chronic Course.*—Cases of tuberculous pleurisy occur in which the onset is abrupt, with pain in the side, fever, cough, and sometimes with a chill. The possibility of their tuberculous nature may not be considered, as the patient may be in excellent physical development and the family history may be good. There is nothing in the course of the disease to at first excite suspicion. Owing to the accumulation of fluid, repeated aspirations may be necessary, and the patient finally recovers from the attack with or without a thickened pleura. The pleurisy may recur, and the case becomes one of chronic pleurisy with thickening of the membranes, whilst eventually the true nature of the disease is manifested by the discovery of definite tuberculous lesions in the lungs and possibly also in other parts of the body.

(*b*) *The Secondary and Terminal Acute Tuberculous Pleurisy.*—Cases of general miliary tuberculosis in which the pleural membranes are involved with other parts do not come under this heading. A miliary eruption is very often secondary to a local tuberculosis in the lung, and under these circumstances the exudate is usually fibrinous. It must be remembered, however, that a pleurisy in the course of a pulmonary tuberculosis is not always due to the presence of tubercles. Post-mortem we certainly see acute miliary tuberculosis of the pleura most frequently in the subjects of some chronic malady—affections of the heart and arteries, chronic Bright's disease, and scleroses of various sorts. Generally there are found old foci of tuberculous disease somewhere in the body, a caseous nodule at the apex of one of the lungs or in the bronchial or mesenteric glands. Attention has, in recent years, been repeatedly directed to the association of tuberculosis of the serous membranes, most commonly of the peritoneum, with cirrhosis of the liver, but a number of instances of terminal tuberculosis of the pleura as well have come under my care in this disease, and it may exist without having caused sufficient symptoms to arouse attention.

(*c*) *Acute Tuberculous Suppurative Pleurisy.*—It has been recognized that a considerable number of the purulent pleurisies designated as latent and chronic depend on tuberculosis, but it is not so generally known that acute ulcerative and suppurative disease of a most severe type may occur and run a very rapid course. Here, also, the onset of the disease is often abrupt, with pain in the side, cough, fever, and not infrequently a chill, and no suspicion of its tuberculous nature is at first entertained.[1]

2. SUBACUTE AND CHRONIC TUBERCULOUS PLEURISIES.—The cases under this heading group themselves into two classes—those with effusion, and the chronic adhesive form, the former being the most common.

(*a*) *With Sero-fibrinous Effusion.*—The affection may be primary, or at least most extensive in the pleura, or secondary to manifest tuberculosis of the lungs. This forms a most important division of the tuberculous pleurisies, and comprises a considerable proportion of all the cases with insidious onset and chronic course. The true character of the disease is often overlooked, and, although it is spoken of as primary in the pleura, in almost every instance there are tuberculous foci in the lungs or bronchial glands or the process has extended from the peritoneum. There are cases in which the termination is in pulmonary tuberculosis or general miliary tuberculosis. In these cases the sero-fibrinous effusion often has a greenish tint, and is sometimes a little turbid. Bacteriologically, the exudate is commonly sterile, though occasionally tubercle bacilli are found in considerable numbers.

(*b*) *With Purulent Exudate.*—The acute form already spoken of is very rare. Much more frequently it is subacute in onset, chronic and latent in its course. The effusion is usually sero-purulent, thin, and often contains a large amount of fatty matter.

(*c*) *Chronic Adhesive Tuberculous Pleurisy.*—This form, characterized by an enormous thickening of the pleural layers, may exist as a primary proliferative process, in which the tubercles, developing in the pleural membranes, cause an early adhesion of the surfaces, and there is at no time much, if any, serous exudate. With the gradual developnent of the tubercles the layers become greatly thickened, measuring om 1 to 2 cm. or more in diameter, and on section they are seen to made up of diffuse tuberculous tissue, with sometimes caseous layers d great development of fibrous tissue. With the exception of the olvement of the bronchial glands this may be the only tuberculous ease in the body. The affection may be limited to one side or bilat- al. Much more frequently, with very great thickening, and perhaps the upper zone union of the pleural membranes, there is separation the layers below and on the diaphragmatic surface by an exudate, ually sero-fibrinous, but sometimes containing curdy or even cheesy aterial. It may be extremely difficult to recognize on first examina- on that the process is tuberculous. A chronic tuberculous pleurisy may exist for a long time and lead to great thickening, without any extension of the fibroid process into the lung: only in very rare instances do the fibroid processes of the pleura invade the lung tissue and lead to extensive sclerosis.

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[1] For a remarkable illustrative case see my *Shattuck Lecture*, 1893.

3. AS A PART OF A GENERAL SEROUS MEMBRANE TUBERCULOSIS, a form which will be considered later. (See p. 774.)

Tuberculous pleurisy secondary to disease in the lungs is of very frequent occurrence. Adhesions and a chronic pleurisy result, which in some instances may be simple, but usually tubercles are scattered throughout the adhesions. An acute pleurisy with effusion may result from direct extension from the lungs. The pleural exudate may be sero-fibrinous or hemorrhagic or may become purulent. Finally, a very common occurrence in pulmonary tuberculosis is the perforation of a superficial spot of softening, with the production of a pyo-pneumothorax.

In a majority of cases the pleura is directly infected from the lung, in other instances from tuberculous glands in the mediastinum or from cold abscesses in the thoracic wall. There may be a direct infection of the lymphatic system. A majority of us inhale tubercle bacilli from time to time. Should any of these escape the phagocytes of the bronchial tree or of the alveoli, they pass through the openings in the latter and reach the alveolar stroma. Those which reach the most superficial air cells may pass into the wide subpleural lymph spaces. It is stated that there is an intimate connection between these lymph spaces and the pleural sac, so that it is quite possible to conceive of a direct entrance of the bacilli into the pleura. More commonly, however, the disease spreads from a subpleural nodule or lymph node in which tubercle bacilli have overcome the tissue resistance and have set up a local tuberculous focus. Hernandez has studied the subject of pleural infection from tuberculous foci in the vertebral or cervical lymph glands. Owing to the wide communication which exists between the lymphatics of the peritoneum and those of the diaphragmatic pleura and mediastinum, it is quite apparent that infection from the peritoneal cavity may readily take place. In rare instances the tuberculous process may result from direct extension from tuberculous disease of neighboring bones.

DIAGNOSIS.—The diagnosis of tuberculous pleurisy often presents great difficulties. Neither the appearance of the individual, the family history, the mode of onset, the course, nor the character of the ex may in any way be suggestive. The groups of lymph glands contiguous to the pleura should be thoroughly examined. Repeated examinations of the sputum should be made, as not infrequently doubtful cases are cleared up by the finding of bacilli, which may come from a very small focus of softening tubercle in connection with a bronchus. Although there is nothing pathognomonic in the macroscopical appearance of the exudate, yet, as already stated, it may present suggestive features. The negative result on bacteriological examination favors the tuberculous nature. The most suspicious instances are those in which the fluid constantly recurs in spite of repeated tappings, and in which, with apparent diminution in the amount of the exudate, the flatness persists, with shrinkage of the affected side.

(2) **Tuberculosis of the Pericardium.**—On both the epi- and pericardium miliary tubercles are not infrequently found in cases of general infection. Extensive tuberculous disease, causing great thickening of the membranes or exudate, is much more common than is supposed and is often overlooked.

(*a*) *Acute Tuberculous Pericarditis.*—This is caused most commonly by direct invasion of the membrane from a tuberculous lymph gland. Less frequently it is due to direct extension from the lung, and it may develop also as a secondary infection from caseous masses in other parts. While usually sero-fibrinous, the exudate is in many cases hemorrhagic. The tubercles are often small, and unless carefully sought for readily overlooked. The exudate may become purulent: the membranes thicken, and the nature of the trouble may not be evident without microscopical examination. The purulent tuberculous effusion in these cases may be enormous, and the condition has frequently been mistaken for pleurisy. In a case reported by Musser the pericardial sac contained 64 ounces of pus.

(*b*) *Chronic Tuberculous Pericarditis.*—This may occur in association with caseation of the bronchial glands or more frequently of the anterior mediastinal lymph glands. Other instances are associated with tuberculosis of the pleura or of the lung. Sometimes the pericarditis is only a part of a general infection of the serous membranes. Occasionally it is due to extension of tuberculous disease from the sternum or from the spine.

The disease is met with at all periods of life, and among my cases there was a child of five years and a man of seventy-two years of age. The layers of the pericardium are thickened, and present cheesy masses or diffuse infiltrated tubercle. The membranes are closely adherent, and in the fibrous connective tissue between the thickened layers (which has often a grayish red appearance) there may be miliary tubercles.

We may recognize four groups of cases of tuberculous pericarditis:

First, those in which the condition is entirely latent, and the disease is discovered accidentally in individuals who have died of other affections or of chronic pulmonary tuberculosis.

A second group, in which the symptoms are those of cardiac insufficiency following the dilatation and hypertrophy consequent upon a chronic adhesive pericarditis. The symptoms are those of cardiac dropsy, and suggest either idiopathic hypertrophy and dilatation, or, if there is a loud blowing systolic murmur at the apex, mitral valve disease, either insufficiency or stenosis.[1] The condition of adherent pericardium is usually overlooked.

In a third group the clinical picture is that of an acute tuberculosis, her general or with cerebro-spinal manifestations, which has had its origin from the tuberculous pericardium or tuberculous mediastinal lymph glands.

A fourth group, with symptoms of acute pericarditis, includes cases in which the affection is acute and accompanied with more or less exudation of a sero-fibrinous, hemorrhagic, or purulent character.[2] There may be no suspicion whatever of the tuberculous nature of the trouble.

Diagnosis.—The diagnosis of tuberculous pericarditis is extremely uncertain. In the large group of cases in which the membranes are thickened and united the difficulties are those which pertain to the recognition of adherent pericardium—difficulties which are enormously enhanced by the state of cardiac insufficiency with which these cases usually come under observation for the first time. In children with a history of repeated attacks of rheumatism the bulging præcordium, systolic retraction of the apex region, the fixation of the upper limit of cardiac dulness, and the diastolic rebound speak for adherent pericardium; and if in a case of this sort there has been no history of rheumatism, and if, on the other hand, there are indications elsewhere of tuberculosis, a probable diagnosis may be made. In the cases which set in as acute pericarditis, unless there are evidences of tuberculosis in other parts, as, for instance, in the left pleura or in the peritoneum, or there are signs of local disease in the lung, and tubercle bacilli have been found in the expectoration, the diagnosis cannot be made. The effusion may be equally as great in tuberculous as in rheumatic pericarditis. If paracentesis be performed, the presence of a bloody exudate is decidedly in favor of tuberculosis; once, at least, tubercle bacilli have been found (Kast). The clinical features themselves offer no criteria, though it would seem probable that in the acute cases with sero-fibrinous exudation the course is more protracted and the fever more irregular than in the ordinary forms of pericarditis; and in such a case the development of diffuse signs in the lungs may lead to a strong suspicion that the process is tuberculous.

(3) **Tuberculosis of the Peritoneum.**—Our knowledge of this affection has been much extended of late years, partly owing to the care and attention with which the cases have been studied, and, owing to the facility with which surgeons and gynecologists now explore the abdominal cavity for obscure conditions of all sorts, we have learned a great deal, not only about the mode of origin of the disease, but about the various phases of its evolution.

The disease occurs at all ages. It is very common in children in association with intestinal and mesenteric tuberculosis. It may occur in advanced life. I have described a case in a patient eighty-two years of age. Of 357 cases which I have collected from the literature,[3] there were under ten years, 27; between ten and twenty, 75; from twenty to thirty, 87; from thirty to forty, 71; from forty to fifty, 61; from fifty to sixty, 19; from sixty to seventy, 4; above seventy, 2.

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[1] There are cases of adherent pericardium in which a bruit is heard which resembles the rumbling presystolic murmur (Hale White).

[2] For illustrative cases of the different clinical forms see *American Journal of the Medical Sciences*, January, 1893.

[3] *Johns Hopkins Hospital Reports*, vol. ii.

It is generally stated that males are more frequently attacked than females. In the recently collected statistics females predominate, owing to the frequency with which laparotomy has been performed for this condition. In America it is a more common disease in the negro than in the white race.

The process may be primary in the peritoneum and confined to this membrane, which was the case in 5 of 17 post-mortem examinations. In a very considerable proportion of all the cases the disease is secondary to tuberculosis of the Fallopian tubes; in a smaller number of cases to affection of the vesiculæ seminales and prostate. Tuberculous salpingitis is an extremely common disease. In my colleague Kelly's department there were examined anatomically, by Dr. Cullen, 12 specimens during a period of twenty-seven months.

J. Whitridge Williams has also shown that certain forms which look like ordinary salpingitis show on microscopical examination the presence of tubercles.

Another common method of infection is through the intestines, and some of the most severe cases are those in which the disease has followed a primary tuberculosis of the bowel. Some authors have insisted specially upon the great frequency of infection from the bowel, though it is probably not of equal importance, in women at least, to infection from the tubes.

In another group of cases the infection seems to be through the lymphatics, and the peritoneum is involved, with the pleural and pericardial surfaces, in a general serous membrane tuberculosis.

It is interesting to note that certain morbid conditions of the abdominal organs predispose to the development of the disease; thus patients with cirrhosis of the liver very often die of an acute tuberculous peritonitis. The frequency with which the condition is met with in operations upon ovarian tumors has been commented upon by gynecologists. Many cases have followed trauma of the abdomen. A very interesting feature is the development of tuberculosis in hernial sacs. The condition is not very uncommon.[1] In a majority of the instances the condition has been found accidentally during the operation for radical cure or for strangulation. In 7 instances the sac alone was involved.

Three forms may be recognized:

(*a*) *Acute Miliary Tuberculosis.*—This form may be latent or form part of a general tuberculosis, and the abdominal symptoms may not attract attention, but in other cases the symptoms from the outset are those of an acute peritonitis. On opening the cavity post-mortem there is usually a sero-fibrinous or sero-sanguineous exudate, rarely purulent, which may be in large amount. The entire membrane is covered with miliary granulations of various sorts, which are fresh and usually surrounded by zones of hyperæmia. In a few of the very acute cases the process is really ulcerative, and there are, without much exudate, tubercles which have rapidly undergone softening—an anatomical condition the counterpart of that which has been described in the pleura as acute cerative tuberculous pleurisy. In a few of these cases tuberculous sions have not been found elsewhere, but in a large proportion of the bjects the disease is secondary. The symptoms of the acute form are ry varied. The onset may be so sudden that the diagnosis of enteritis of hernia is made, and in one case an operation for strangulated her- was performed. More frequently the acute symptoms of the onset ead to the diagnosis of a simple peritonitis. The patient complains of dominal pain; there is tenderness on pressure and the symptoms of cites gradually develop. In a large group of cases the onset is more dual, and the general symptoms overshadow entirely the local condi- n. The fever, slight abdominal tenderness, the tympanites, and the ronic course and low typhoid state lead very frequently to the diagnosis of enteric fever. In other acute cases the disease sets in with the most persistent vomiting. Acute pleurisy sometimes develops. The fever is variable. It is usually a marked symptom in the acute cases, in which the temperature may reach 103° or 104° F. In this form of the disease recovery may occur, either spontaneously or after laparotomy.

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[1] See *Bruns' Beiträge*, Bd. xi.

(*b*) *Chronic ulcerative tuberculosis*, perhaps the most common form of the disease, is characterized by the presence of larger growths, which tend to caseate and ulcerate and which may lead to perforation of the intestinal coils. The exudate is sero-purulent or purulent; in other instances it has a slightly chocolate color or may have a fatty appearance. It is often sacculated. The abdomen is usually prominent and tender, and nodular masses can be felt. Adhesions sometimes take place about the navel, and there is a redness or a region of infiltration; sometimes there is periumbilical suppuration, and a discharge of pus takes place. The fever is usually irregular, and, when there is much suppuration or encapsulated pockets of pus, may have a hectic character. Low temperatures are not so common in this type as in the chronic fibrous form. Walter Channing made a very interesting study of the temperature in a case of tuberculosis of the tubes, with tuberculous pelvic abscess and perforation into the rectum and chronic tuberculosis of the peritoneum and mesenteric glands. The temperature was recorded for a period of two years and three months. The total number of observations amounted to 1582: 409 times there was a rise between 100° and 102°; 87 times there was a rise between 102° and 105°; twice 105° and several times 104.4° was reached. Ascites may occur in this variety, but the exudate is rarely in large amount and is usually sero-purulent.

(*c*) *Chronic Fibroid Tuberculosis.*—In this variety the tubercles are hard and sclerotic, often surrounded by areas of pigmentation; the membranes are usually agglutinated and the omentum is puckered and rolled into a firm, hard mass. The form is not infrequently found as an accidental condition in persons who have died of other diseases. It is in this chronic fibroid type that we most frequently see deep pigmentation of the skin, which may be so pronounced as to lead to the diagnosis of Addison's disease. The temperature may be subnormal, and for weeks at a time the morning temperature may not be above 96° or 97°. This form is very frequently associated with chronic fibroid tuberculosis of one apex.

There are several points about tuberculous peritonitis which require special consideration. Of these the most important is the formation of tumor-like bodies. These may be—

(*a*) *Omental,* due to puckering and rolling of this membrane until it forms an elongated firm mass attached to the transverse colon and lying athwart the upper part of the abdomen. This cordlike structure is found also with cancerous peritonitis, but is much more common in tuberculosis. Gairdner has called special attention to this form of tumor, and in children has seen it undergo gradual resolution. A resonant percussion note may sometimes be elicited above the mass. Though usually situated in the umbilical region, the omental mass may form a prominent tumor in the right iliac region.

(*b*) *Sacculated exudation,* in which the effusion is limited and confined by adhesions between the coils, the parietal peritoneum, the mesentery, and the abdominal or pelvic organs. This encysted exudate is most common in the middle zone, and has frequently been mistaken for ovarian tumor. It may occupy the entire anterior portion of the peritoneum, or there may be a more limited saccular exudate on one side or the other. It may lie completely within the pelvis proper, associated with tuberculous disease of the Fallopian tubes.

(*c*) *In rare cases* the tumor formation may be due to great retraction or thickening of the *intestinal coils.* The small intestine is found shortened, the walls enormously thickened, and the entire coil may form a firm knot close against the spine, giving on examination the idea of a solid mass. Not the small intestine only, but the entire bowel from the duodenum to the rectum, has been found forming such a hard nodular tumor.

(*d*) *Mesenteric glands,* which occasionally form very large, tumor-like masses, more commonly found in children than in adults. This condition may be confined to the abdominal glands. Ascites may coexist. The condition must be distinguished from that in children, in which, with ascites or tympanites—sometimes both—there can be felt irregular nodular masses, due to large caseous formations between the intestinal coils. No doubt in a considerable number of cases of the so-called tabes mesenterica, particularly in those with enlargement and hardness of the abdomen—the condition which the French call *carreau*—there is involvement also of the peritoneum.

Another important event in tuberculous peritonitis is the occurrence of occlusion of the bowel, which may be due either to contraction of fibroid bands or to a kink in the bowel caused by adhesions. In other cases there has been chronic ulcerative disease of the mucous membrane, with secondary involvement of the peritoneum and cicatricial contraction of some of the ulcers. It is possible, too, that the great retraction and thickening of the intestinal coils may lead to symptoms of obstruction, while in other instances the acute tuberculous peritonitis may cause such infiltration of the muscular coats as to induce a paralytic distention.

The diagnosis of tuberculous peritonitis is often very easy. In other cases it is extremely complicated. The only general disease with which it is apt to be confounded is typhoid fever. The slow onset, the slight abdominal symptoms, the local tenderness, and the gastric features often suggest enteric fever. The gradual development of the ascites or the presence of nodular masses may be the first symptom to suggest a local peritonitis. In the ascitic form the diagnosis may rest between an acute miliary cancer, cirrhosis of the liver, and a chronic simple peritonitis—conditions which usually offer no special difficulties in differentiation. A most important point is the simultaneous presence of a pleurisy. The diagnosis of the peritoneal tumors in this affection is sometimes very difficult. The omental tumor is a less frequent source of error than any other, but a similar condition may occur in cancer. The diagnosis of the saccular exudate from ovarian tumor is now made much more frequently than a few years ago. The most suggestive points for consideration are the history of the patient and the evidence of old tuberculous lesions. The physical condition is not of much moment, as in many instances the patients have been robust and well nourished. Irregular febrile attacks, gastro-intestinal disturbance, and pains are more common in tuberculous disease. Unless inflamed, there is usually not much fever with ovarian cysts. The local signs are very deceptive, and in certain cases have conformed in every particular to those of cystic disease. The outlines in saccular exudation are rarely so well defined. The position and form may be variable, owing to alterations in the size of the coils of which in parts the walls are composed. Nodular cheesy masses may sometimes be felt at the periphery. Depression of the vaginal wall is mentioned as occurring in encysted peritonitis, but it is also found in ovarian tumor. Lastly, the condition of the Fallopian tubes, of the lungs, and of the pleuræ should be thoroughly examined. The association of salpingitis or epididymitis with an ill defined anomalous mass in the abdomen should arouse suspicion, as should also involvement of the pleura or the apex of one lung.

(4) **General Serous Membrane Tuberculosis.**—There is a group of cases of tuberculosis in which the serous membranes are chiefly involved, either simultaneously or more commonly one after another, forming a clinical type fairly distinctive and readily recognized. There have been several interesting studies of this condition, notably the Paris Theses of Moran and Boulland in 1884 and 1885 and the careful study of Vierordt.[1] The pleuro-peritoneal membranes may be alone involved or the pleuro-peritoneal and pericardial surfaces. There are, as noted by Boulland, three groups of cases: First, an acute tuberculosis, with rapid evolution of the disease in pleuræ and peritoneum, generally consecutive to local disease of the tubes in women, or of the mediastinal or bronchial lymph glands.

Second, cases in which the disease is more chronic in its nature, with exudation in both peritoneum and pleuræ, the formation of cheesy masses, and the occurrence of ulcerative and suppurative processes. In this group the pleural involvement is much more commonly secondary to the peritoneal, or both may be a sequence of pulmonary tuberculosis.

And, third, there are instances in which the pleuro-peritoneal affection is still more chronic, the tubercles hard and fibroid, both the membranes showing much thickening, often with very little exudation.

A knowledge of the existence of this combined infection is somewhat important, as the cases are often of great obscurity. More commonly the affection begins in the peritoneum and may be extremely chronic, and then gradually invades the pleura. In other instances there is a subacute pleurisy and subsequent invasion of the peritoneum. The cases often have a very protracted course; there are periods of great improvement and there may be little or no fever.

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[1] *Zeitschrift für klinische Medicin*, Bd. xi.

IV. TUBERCULOSIS OF THE LUNGS (PHTHISIS; CONSUMPTION).

I. Acute Pneumonic Phthisis.

Synonyms.—Tuberculous infiltration (Laennec); Caseous pneumonia; Scrofulous pneumonia (Virchow).

Two main types are recognized—the pneumonic and the bronchopneumonic. The former is more common in adults, the latter in children. The disease is apt to attack persons who have been debilitated by previous illness or weakened by exposure and dissipation. Either form may, however, occur in persons in apparently good health.

Pathology and Morbid Anatomy.—This acute form of pulmonary disease, also known as *phthisis florida* and galloping consumption, is essentially an aspiration tuberculosis.

In nearly all instances the disease is secondary to a pre-existing tuberculous focus, most frequently in the lung itself, either an apical cavity, often of very small size and usually communicating freely with a bronchus, or a softened gland has ruptured into a neighboring bronchus.

In the pneumonic type a whole lobe, or even a whole lung, is involved, while in the broncho-pneumonic only lobules or collections of lobules are affected. According to the observations of Prudden, this varying distribution of the lesions would seem to depend partly upon mechanical causes and partly upon the number of tubercle bacilli distributed from the infecting area, as he was able by regulating the dosage and the method of distribution to produce experimentally either the lobar or lobular form. When in his experiments relatively small quantities of the bacilli were introduced into the lung, and care was taken to distribute them equally throughout the organ, small discrete areas of consolidation resulted. When larger quantities of bacilli, in larger amounts of fluid, were introduced, and no great effort was made to bring about an equal distribution of the suspension, large areas of consolidation, resembling the areas of pneumonic tuberculosis in man, resulted. According to Fränkel and Troje, the morphological differences between the so-called cheesy pneumonia, which is a tuberculous broncho-pneumonia, and the organized tissue structures known as tubercles is primarily due to the fact that while the tubercles are developed in the interalveolar structures of the lungs, to which the bacilli are brought by the blood or lymph vessels, largely free from intermingled poisonous substances, the infection by aspiration is intra-alveolar, and the bacilli are accompanied by greater or less quantities of diffusible poisonous material developed at their original seat. Thus, while in the vicinity of metastatic tubercles, miliary or otherwise, the metabolic products of the growth of the tubercle bacillus gradually produced may incite exudation and cell proliferation beyond the limits of the focus of productive inflammation, this is not, and cannot be, so extensive and quickly developed as under conditions which involve the sudden acces- ion to the air spaces of the lungs not only of tubercle bacilli, but of eater or less quantities of already elaborated poison, as is the case the tuberculous broncho-pneumonia of acute phthisis incited by iration.

Notwithstanding this community of causation, the types of the disease present certain differences, both clinically and pathologically, that leserve separate description.

(*a*) *The Pneumonic Form.*—On removal of the lung the portion ffected does not collapse, but is solid and airless. The overlying eura is usually covered by a layer of exudate, either fibrinous or case- us, of varying thickness. The appearances on section vary considerably according as the exudative or the tubercle element predominates. When the former only is present, with but slight formation of actual tubercle nodules, the gross appearances can, in the earlier stages, almost exactly resemble those seen in croupous pneumonia, though a close search will almost invariably reveal the presence of miliary tubercles in the consolidated area. In other cases, when the formation of actual tubercles is on a par with or exceeds the exudative process, the appearance on section is somewhat different. The cut surface does in a manner resemble that seen in lobar pneumonia in that it is studded with granulations, which, however, are larger and smoother than those seen in the disease mentioned. On close inspection these granules are seen to be miliary tubercles, and the surrounding lung may present the appearances of an ordinary pneumonia, or, more commonly, those associated with desquamative pneumonia—viz. a reddish gray, very translucent appearance. These appearances of desquamative pneumonia or of ordinary croupous pneumonia may often be combined in the same lung, certain areas showing one variety, whilst the other variety is seen in adjacent or distant areas. In the later stages of the disease the picture is much more characteristic; but the origin of the process in the nodular or exudative form cannot be made out with the naked eye, the subsequent caseation having masked the original lesion. The appearance of the cut surface at this time has been described as resembling Rochfort cheese—a whitish yellow background streaked with blackish lines, the background representing the caseous material, the streakings the pigmented bands of connective tissue. Occasionally cavities are seen with ragged, necrotic walls. These are probably, for the most part, due to secondary infection of the tuberculous tissue with pus-producers.

Various intermediate steps can be seen between the early and caseous stages as above described; the process is not, as a rule, uniform, so that the lungs are frequently seen presenting a mixture of the above appearances, in parts caseous, in parts gelatinous, and in parts showing tubercle nodules.

The bronchi in all these cases, particularly the smaller ones, usually show evidences of active inflammation in a congested and thickened mucous membrane and purulent or muco-purulent contents.

The tubercle nodules as seen in these lungs differ in no respect from those seen elsewhere and previously described. The exudative phenomena vary within very wide limits, but the essential elements of the exudate are in all cases the same—red and white (polynuclear and mononuclear) corpuscles of the blood, the blood serum, fibrin, and the epithelial cells lining the alveoli. The exudate may resemble that seen in croupous pneumonia, containing large numbers of red corpuscles or large quantities of fibrin, and in fact any of the various combinations of the above described essential elements may occur. The most typical form of pneumonia, however, is that first accurately described by Laennec as gelatinous pneumonia—a form in which the exudate consists of an albuminous fluid derived from the blood and greater or smaller numbers of cells of an epithelioid type originating from the desquamation and proliferation of the epithelial lining of the alveoli. The appearances under the microscope in the last stage are those of large areas of caseation surrounded by larger or smaller areas, either of one of the types of pneumonia above mentioned or of tubercle formation.

(*b*) *The Broncho-pneumonic Type.*—Little need be said of this type, which occurs more frequently in children than in adults. As has been stated above, the difference between this and the preceding form is merely one of degree. Here, as in the pneumonic, we have the differences in appearance according to the stage of the disease and according as the exudative or nodular elements predominate. The sole difference lies in the distribution of the lesions, which in this class of cases are confined to limited areas of lung substance, generally in the neighborhood of small bronchi.

In connection with both these forms of tuberculosis it is necessary to discuss the question of associated or secondary infections in acute lung tuberculosis. Can all the above described changes be due to the action of the tubercle bacillus itself or are they due to mixed infections? The careful observations of Fränkel and Troje would seem to support the view of the specificity of the tubercle bacillus, whilst the equally careful studies of Ortner appear to negative these results. The recent researches of Prudden would seem to put the matter beyond all question of doubt. This observer was able to show in the clearest manner that the tubercle bacillus could produce not only distinct tubercle nodules, but also the various kinds of exudative phenomena, the exudates varying in appearance in different cases, which phenomena occurred absolutely without association with other organisms. The fact that these latter had not subsequently crept in was shown by cultures at the autopsy on the affected animal.

SYMPTOMS.—(*a*) *Pneumonic Form.*—In many cases the disease sets in abruptly with a chill, which may follow an exposure to cold or come on in the course of a drinking bout (Fränkel and Troje); in others the disease sets in more insidiously. The temperature rises quickly, and there are all the initial symptoms of ordinary pneumonia—pain in the side, cough, and shortness of breath. Usually by the time a physician sees the case hepatization is well marked, and he discovers an area of consolidation in a lower lobe or in an upper lobe, with possibly a friction murmur and loud tubular breathing. The expectoration is usually blood-tinged and typically pneumonic. The local disease progresses, and an entire lobe may be involved or the upper and middle lobe on the right side. Occasionally an entire lung is invaded with great rapidity. No doubt at this time may be in the mind of the physician the nature of the case, which is regarded as one of simple lobar monia. In some instances the previous history of the patient ds warrant for a suspicion which is unheeded in the presence of a characteristic onset. The fever is at first high and persistent, but slight daily variations, but it becomes more irregular as the se progresses. The pulse is rapid, from 120 to 140 beats per te. The respirations are much accelerated at first, but with extenconsolidation and high fever there may be neither urgent dyspnœa nosis. Instead of the expected crisis on the ninth or tenth day, ver persists and becomes more irregular. The expectoration s, is less rusty, and becomes muco-purulent or purulent and of a sh color. There may be no expectoration throughout. In a case my care a few years ago, in which the consolidation was uniform apex to base, there was no expectoration and very little cough. n in the second or third week the physician comforts himself with thought that perhaps it is a case of unresolved pneumonia, and it is until signs of cavity-formation develop or until tubercle bacilli or lastic tissue is detected in the sputa that he becomes convinced of the existence of an acute pneumonic phthisis. A diagnosis may never be reached *intra vitam*, and the case may be sent to the post-mortem room without the slightest suspicion that it is anything but an instance of protracted pneumonia. A violent hæmoptysis may occur at any time in the course of the disease. Among other points which may be mentioned are—enlargement of the spleen, a diazo reaction in the urine, and occasional œdema of the lower extremities. There may be active delirium or only an apathy and dulness proportional to the extent of the fever.

The diagnosis of acute pneumonic phthisis offers many difficulties. The mode of onset may be in every respect identical with that of croupous pneumonia. A healthy, robust-looking young Irishman, a cab-driver, who had been kept waiting for hours on a cold, blustering night, was seized the next afternoon with a violent chill, and the following day was admitted to my wards at the University Hospital, Philadelphia. He was made the subject of a clinical lecture on the fifth day, when there was absent no single feature in history, symptoms, or physical signs of acute lobar pneumonia of the right upper lobe. It was not until ten days later, when bacilli were found in his expectoration, that we were made aware of the true nature of the case. I know of no criterion by which cases of this kind can be distinguished in the early stage.

The presence of the greenish, often grass-green sputa, upon which Traube laid much stress, is a point of a good deal of importance. By far the most valuable information is obtained by a systematic study of the expectoration. The tubercle bacilli, as a rule, are not present at first, and may not be found for a week or ten days or even later. They may be present early, and Fränkel and Troje found them in one case in which the sputa were still pneumonic. The examination for elastic tissue is very important, as in a majority of the cases the caseous areas begin to break early. Traube called attention to the absence of breath sounds in the consolidated region, a point which Herard and Cornil also speak of as important, but suppression or enfeeblement of the breath sounds is by no means uncommon in other types of pneumonia.

The *course of the disease* is very variable. In a majority of the cases death occurs within six weeks. Death may be caused as early as the eighth or tenth day. There are cases in which with very severe onset and rapid consolidation of a lobe the symptoms subside within three or four weeks, and the condition passes into one of chronic phthisis, which does not prove fatal for five or six months or even longer.

(*b*) *Broncho-pneumonic Form.*—In adults the picture is that of a rapidly progressing *phthisis florida.* Persons in good health are rarely attacked, but most frequently those who are debilitated from any cause or convalescent from the acute diseases. Some of the most rapid cases follow hæmoptysis. There may be at the outset repeated chills, with sweats and intermittent pyrexia, which may lead to the diagnosis of malarial intermittent fever. The temperature is high, the pulse rapid, and the cough distressing. The general symptoms may be out of proportion to the amount of local disease. The apices are most commonly involved, and there is at first only slightly impaired resonance, with harsh breathing and numerous fine râles. Subsequently, as the areas coalesce, the resonance becomes still more defective and the breathing may be tubular. In very acute cases the fever may be high. There is early delirium and the patient sinks into the so-called typhoid state. With the progress of the local disease there is rapid loss in weight and strength, irregular fever, sweating, and the sputa show numerous tubercle bacilli and much elastic tissue. The disease may prove fatal within from six to ten or twelve weeks, and a majority of the cases of galloping consumption belong to this type. There are cases in which for five or six weeks the symptoms are of the greatest severity, and the immediate prognosis looks hopeless, but the fever subsides, the constitutional symptoms mitigate, and a case which may have looked desperate drags on and eventually becomes chronic.

The acute tuberculous broncho-pneumonia is a very common form in children, and may come on spontaneously or follow one of the infectious diseases. Clinically, it is very difficult to distinguish from the simple form. The onset may be acute in a previously healthy child or the disease follows measles, diphtheria, or whooping cough. The temperature rises rapidly, the cough is severe, and there may be signs of consolidation with fine crepitant and subcrepitant râles at one or both apices. There are no physical signs which enable us to differentiate a simple form of tuberculous broncho-pneumonia. The localization is not of much value, since we find, commonly enough, in children the tuberculous process beginning at the base or in the central portions of the lung. In the course of the disease indications of value develop. The oscillations in temperature are greater in the tuberculous cases; sweats are more common. The child emaciates rapidly, and there may be local features indicating breaking down of the lung tissue. As young children rarely expectorate, there is great difficulty in getting the sputa for examination. Occasionally they can be obtained in the vomitus, and as the sputum is swallowed the tubercle bacilli can occasionally be determined in the stools. The duration of the very acute cases is from three to five weeks. In other instances the severity of the symptoms mitigates within two or three weeks, but the irregular fever persists;

e is loss of flesh, cough, hectic fever, and sweats. The physical indicate softening, and there is gradually developed a clinical e of chronic pulmonary tuberculosis.

II. Chronic Ulcerative Tuberculosis of the Lungs.

ynonyms.—Phthisis pulmonum; Consumption; Chronic phthisis; ic ulcerative phthisis.

In this form, which embraces by far the largest number of cases of monary tuberculosis, the lesions proceed to caseation and ulceration, d there is produced at last the only too common picture of pulmonary nsumption, characterized by cough, irregular fever, emaciation, night-sweats, etc. Though at first a tuberculous process, in a majority of ses the lungs become the seat [illegible]ed infection, and many of the prominent symptoms are due to the absorption of the toxins of various ganisms in purulent foci and cavities.

Pathological Anatomy.—(1) *The Distribution of the Lesions.*—The primary lesion is, as a rule, in one of the upper lobes, usually at a point a short distance below the apices. The question as to which apex is involved the most frequently has been studied by various authors. The statistics on the subject vary, some claiming that the right, others that the left, side is most often affected, while in other cases the two sides have been equally involved. Of 427 successive cases at the Johns Hopkins Hospital, the right apex was involved in 172, the left in 130, and both in 111.

Various hypotheses have been advanced to explain the cause of this peculiarity of distribution of the lesions, but none are entirely satisfactory. The distribution cannot be explained on mechanical grounds alone, and in our present knowledge of the subject we feel obliged to call in a local weakness of the part or a predisposition, a weakness consisting perhaps in some preceding catarrhal condition. From its original seat near the apex the tuberculous process travels downward with greater or less rapidity toward the base. This process of spreading is in the great majority of cases the result of the aspiration of infected material from already affected regions in the upper part of the lung into the lower bronchi. Associated with this process there is also a gradual dissemination of new tubercles from the old centres. The colonization, radial in character, is due to the carriage of tubercle by the lymph streams. Much more rarely local extension may occur through the blood current.

The tubercles of aspiration origin have their most frequent seat at the point where the bronchioles narrow down just at the entrance to the vestibule of the air sac; they are also found in the walls of the smaller and larger bronchi. Tubercles of blood origin are generally evenly scattered throughout the lung, those of lymph origin occurring near old foci.

The mode of extension has been carefully described by Kingston Fowler, who finds that in its onward progress through the lungs the disease follows, in a majority of the cases, distinct routes. In the upper lobe the primary lesion is not, as a rule, at the extreme apex, but from an inch to an inch and a half below the summit of the lung and nearer to the posterior and external borders. The lesion here tends to spread downward, probably from inhalation of the virus, and this accounts for the frequent circumstance that examination behind, in the supraspinous fossa, will give indications of disease before any evidences exist at the apex in front. Anteriorly, this initial focus corresponds to a spot just below the centre of the clavicle, and the direction of extension in front is along the anterior aspect of the upper lobe, along a line running about an inch and a half from the inner ends of the first, second, and third interspaces. A second less common site of the primary lesion in the apex "corresponds on the chest wall with the first and second interspaces below the outer third of the clavicle." The extension is downward, so that the outer part of the upper lobe is chiefly involved.

In the middle lobe of the right lung the affection usually follows the upper lobe on the same side. In the involvement of the lower lobe the first secondary infiltration is about an inch to an inch and a half below the posterior extremity of its apex, and corresponds on the chest wall to a spot opposite the fifth dorsal spine. This involvement is of the greatest importance clinically, as "in the great majority of cases, when the physical signs of the disease at the apex are sufficiently definite to allow of the diagnosis of phthisis being made, the lower lobe is already affected." Examination, therefore, should be made carefully of this posterior apex in all suspicious cases. In this situation the lesion spreads downward and laterally along the line of the interlobular septa —a line which is marked by the vertebral border of the scapula when the hand is placed on the opposite scapula and the elbow raised above the level of the shoulder. Once present in an apex, the disease usually extends in time to the opposite upper lobe, but not, as a rule, until the apex of the lower lobe of the lung first affected has been attacked.

Lesions of the base may be primary, though this is rare. Percy Kidd makes the proportion of basic to apical phthisis one to five hundred, a smaller number than existed in my series. In very chronic cases there may be arrested lesions at the apex and more recent lesions at the base.

(2) *The Lesions in Chronic Ulcerative Phthisis.*—(*a*) *Tubercles.*—The miliary tubercle is the essential element in the early stages of chronic ulcerative phthisis, the nodules at this time being usually situated at the apex in connection with the air cells and smaller bronchi. As the process proceeds the nodules coalesce and form conglomerate tubercles, the breaking down of which, with the subsequent further destruction of tissue, leads to cavity formation.

When the disease has reached its chronic form the miliary tubercles present in the lung are found, in the great majority of instances, to have one of two distributions: (1) A dissemination due to aspiration of tuberculous material, the tubercles being situated in the air cells or the walls of the smaller bronchi; (2) the distribution due to dissemination of tubercle bacilli by the lymph current, the tubercles being scattered about the old foci in a radial manner. Much more rarely there is a scattered dissemination from infection here and there of the smaller vessels, the tubercles then being situated in the vessel walls.

(*b*) *Pneumonia.*—In all cases of chronic phthisis patches of pneumonia are found distributed through the lung. One form is a

cho-pneumonia, having its origin in the smaller bronchi. The
late in these cases fills up the bronchus and the surrounding
cells, and may present varying appearances. In the beginning
in some cases the ordinary muco-purulent exudate, in some
ious or fibrino-purulent, in others gelatinous. Subsequently, when
exudate undergoes caseation, a cross section of the affected area
n gives the typical appearance of caseous broncho-pneumonia—viz.
bronchus in the centre of the cheesy material, surrounded by an
of lung consolidation, also caseous. The longitudinal section has
mewhat dendritic or foliaceous appearance. As these areas soften
ities are formed; the breaking down is due in most instances to a
ondary infection with pus organisms, though the tubercle bacillus
elf is capable of causing it. In other instances, particularly in very
hronic cases, a chronic interstitial pneumonia is set up in the region
surrounding the caseous mass, with the result that it may be completely
urrounded by a dense fibrous capsule. Under these circumstances the
uid elements of the cheesy mass may be absorbed, and it remains as a
firm, dry, friable nodule, or it becomes the seat of a deposition of lime
salts, and a hard, calcareous mass results.

The second type of pneumonia is not connected with the bronchi, but with the tubercle nodules. This pneumonia may occur at any stage of the tuberculous process, and is often seen surrounding the very youngest tubercles. The exudate is sharply confined to the alveoli in the immediate neighborhood of the tubercles, and where these are closely packed almost the whole of the lung substance between them may be consolidated. Here, as in the acute pneumonic tuberculosis, the exudate may be of varying types, the essential elements being the serum, leucocytes, and red corpuscles of the blood, together with fibrin and the desquamated and proliferated alveolar epithelium. The proportion of these elements varies greatly, but, though the type of exudate may simulate any form of pneumonic exudate, by far the most common variety in these cases is the gelatinous (described by Laennec), an exudate containing often but few cellular elements, and these mostly epithelial in character. The number of tubercle bacilli found in such an exudate is very small indeed, and from the arrangement of the pneumonic patches about tubercles and their sharp localization it seems probable that the exudate is due to the products of the tubercle bacillus, and not to the organism itself.

The exudate in this form of pneumonia may undergo caseation or fatty degeneration, the former much more frequently. The caseous material presents the same appearance here as elsewhere; the fatty degenerated alveolar contents have a whitish or yellowish white opaque appearance.

(*c*) *Cavities.*—Two kinds of cavities are found in the lung in chronic phthisis—the bronchiectatic and the ulcerative.

Though not necessarily of tuberculous origin, bronchiectatic cavities are frequently met with, most commonly at the apices of the lungs, for the reason that the tuberculous process is most common there. The cavities are found particularly in connection with the medium sized and small bronchi, and vary in size from a pea to a hen's egg; pure bronchiectatic cavities, however, rarely reach the latter size. The shape varies considerably: in some instances a long stretch of bronchus is diffusely dilated, causing a fusiform cavity; in other instances only a part of the bronchial wall gives way, causing a sacculated cavity. In another class of cases sharply defined dilatations occur, taking in the whole bronchial circumference and causing a localized globular cavity. In all the wall of the cavity is, as the name implies, of bronchial origin, usually sharply defined and smooth on its inner surface, though the granulation tissue which lines it may be the seat of more or less extensive ulceration. In the larger cavities the ulcerative process generally extends beyond the bronchial wall and involves the lung substance, and we have a combination of the bronchietatic and ulcerative forms of cavities.

The ulcerative cavity may occur in one of two ways—either as the result of an extension of the ulcerative process from a bronchiectatic cavity into the lung, or from the breaking down of tuberculous masses in the lung irrespective of connection with bronchi. In both of these cases it is probable that the destructive process results in most instances from an invasion of a tuberculous lung by the pus organisms, particularly the streptococcus, though, as the work of Prudden has shown, the bacillus of tuberculosis is capable itself of causing ulcerative processes of limited extent. The ulcerative cavities, like the bronchiectatic, are most frequently found at the apices, though in late stages of the disease they may be scattered through the lungs. They vary in size from cavities the size of a marble to those involving a whole lobe or even a whole lung, in some instances only a thin shell of a lung remaining outside of the cavity. A majority of these cavities communicate with bronchi by openings of various sizes and having varying positions.

The appearance of the ulcerative cavity differs in the acute and chronic stages. The acute form, which is seen in acute phthisis, and in chronic phthisis in those parts of the lung in which the disease is progressing, is distinguished from the chronic by its lack of a definite wall, and is bounded only by broken-down caseous material and necrotic lung tissue. In the caseous tissue of the fresh lung cavity tubercle bacilli are often present in enormous numbers. As the process of formation of these cavities is acute, they are the form especially liable to rupture into the pleura and cause pneumothorax.

The chronic form differs from the acute in having a definite wall, composed in the main part of dense fibrous tissue, the result of a chronic interstitial pneumonia in the surrounding lung. Inside this framework is a layer of granulation tissue, which shades gradually into the fibrous layer, and may contain tubercles or show caseation of its most internal portion. At times no definite tubercles can be made out, but the tissue may present the microscopical appearances spoken of as tuberculous granulation tissue, the process consisting in a diffuse infiltration with epithelioid cells and occasionally giant cells. The walls of such cavities are generally extremely irregular, being crossed by bands representing resistant areas of dense fibrous tissue or the remains of bronchi or bloodvessels. The cavities are often crossed from side to side by trabeculæ in which, as in those of the walls, are bloodvessels, many of which are obliterated, either as a result of an endarteritis or by an atrophy, following the destruction of the tissues which they supply. In many instances, however, obliterative process does not take place, and the bloodvessels, being more resistant to the ulcerative process than the surrounding tissue, remain exposed, either in the wall of the cavity or in one of the bands crossing it. In these exposed vessels, devoid of their normal support, aneurysms are particularly liable to form, varying in size from a pea to a walnut, and their rupture in the later stages of the disease is the most common cause of profuse hæmoptysis.

The extension of the cavities takes place by the gradual ulceration of their inner walls, which occurs in a patchy manner, some portions of the wall being resistant, whilst others, especially those containing caseous tubercles, are easily broken down.

The contents of the cavities consist of broken-down tissue (caseous material or destroyed lung tissue) and pus secreted from the lining wall; more or less blood may be present from the rupture of small vessels.

In the most chronic forms of tuberculosis, where the reparative tends to exceed the destructive processes, cavities become surrounded by an exceedingly dense fibrous wall and a cessation of the ulcerative process may occur. Such cavities, termed quiescent, have smooth, almost fibrous walls, which secrete practically nothing. They may undergo contraction by the shrinking of the outlying fibrous tissue, but, except in very small ones, complete obliteration does not occur.

(*d*) *Involvement of the Pleura.*—The pleura is involved to a greater or less extent in all cases of tuberculosis, either in an acute or chronic process. In the acute form the various types of exudate may occur, the sero-fibrinous being the most common. A large number of the pleural exudates, which are bacteriologically sterile, are of a tuberculous origin. Purulent and hemorrhagic exudates are less often found; in the case of the former the polynuclear leucocytes may contain large numbers of tubercle bacilli. Definite tubercles are not necessarily associated with any of these processes, though in the great majority of instances they will be found if carefully looked for. Here, as in other forms of pleurisy, complete return of the pleura to normal does not take place. In many instances partial or entire obliteration of the pleural sac occurs from the adhesions and subsequent organization of the exudate: in other cases, particularly in connection with the more acute forms of phthisis, the exudate undergoes extensive caseous changes. The pleurisy is quite commonly secondary to a pneumothorax.

The chronic forms of pleurisy are, as a rule, more sharply localized than the acute, though they often spread, coincident with the spread of lung involvement. They almost invariably result in adhesions between the two layers of exudate, which subsequently undergo organization and may become extremely dense and firm.

(*e*) *Changes in the Bronchi.*—The larger bronchi are generally the seat of inflammation, acute or chronic in character and due to organisms other than the tubercle bacillus. Besides these non-specific lesions, tuberculous lesions occur, either in the form of tubercles in the mucous membrane or of ulcerations varying from small superficial losses of substance to large serpiginous ulcerations, involving at times all the coats and leading to dilatation of the bronchus. The medium-sized bronchi are also subject to both nodular and ulcerative processes. As has been previously mentioned, the smaller bronchi are the starting point in most cases of lung tuberculosis, and show various lesions due to the action of the tubercle bacillus, most of which have been already described. Besides these specific lesions, they may be the seat, especially in children, of inflammation due to secondary invasion, most frequently by the micrococcus lanceolatus, with the production of a bronchopneumonia.

(*f*) *Lesions in the Bronchial Glands.*—The lymph glands are involved in almost all cases of pulmonary tuberculosis. In some instances only one or two glands show signs of the disease, and in others, particularly in children, the whole of the bronchial group may be converted into a dense caseous mass which extends deep into the roots of the lungs. In the adult the process is usually less extensive, beginning with a few tubercles in the gland: caseation follows, and in a large number of instances calcification subsequently occurs. Secondary changes are not very common, but infection with the pus organisms may be followed by abscess, which may break into a bronchus, the pleura, the trachea, the œsophagus, or even into the blood current.

(*g*) *Changes in Other Organs.*—The changes occurring in other organs secondary to pulmonary tuberculosis may be due to—(*a*) direct extension of the disease process; (*b*) dissemination by the blood or lymph currents of the tubercle bacillus or secondary invading organisms; (*c*) dissemination of tuberculous products by the alimentary canal; (*d*) dissemination of toxins.

The changes due to the direct extension of the disease are seen particularly in the respiratory tract, in the bronchi, as mentioned above, and in the trachea and larynx, all of which may show tuberculous lesions, either in the form of tubercles or of ulcerative processes. Under this head would come also certain cases of tuberculous pericarditis, the extension taking place by way of the pleura. A certain number of tubercle bacilli no doubt reach the circulation in every case of lung tuberculosis: they originate in the various organs the scattered tuberculous foci which are seen at every autopsy on cases of lung tuberculosis. The endocarditis associated with lung tuberculosis is also due to blood infection, and may be caused by the tubercle bacillus alone or the secondary invaders, or may be a mixed infection.

The sputa are responsible for the lesions of the buccal tract, and when swallowed may cause lesions in the œsophagus, stomach, and intestine.

The amyloid degeneration of certain organs, and perhaps also the peculiar bone changes occasionally seen, are probably due to the absorption of toxins, but whether derived from the tubercle bacilli themselves or from secondary invaders must remain a matter of conjecture.

The importance of secondary infections in tuberculosis is apparent when we consider what a large percentage of patients show at autopsy general infection with the pus organisms.

SYMPTOMS.—*Modes of Onset.*—No one of the protean features of pulmonary tuberculosis is more striking than the diverse ways in which the disease may begin. Among the more important of these are the following:

(*a*) There is a small but important group of cases in which the disease makes considerable progress before there are serious symptoms to arouse the attention of the patient. This latent form of the disease is seen most frequently in workingmen, and the disease may even advance to excavation of an apex before they seek advice. In some of these cases it is not a little remarkable how slight the lung symptoms have been.

A different type of latent pulmonary tuberculosis is the form in which the symptoms are masked by the existence of serious disease in other organs, as in the peritoneum, intestines, or bones.

(*b*) *With Symptoms of Dyspepsia and Anæmia.*—The gastric mode of onset is very common, and the early manifestations may be great irritability of the stomach with vomiting or a type of acid dyspepsia with eructations. In young girls (and in children) with this dyspepsia there is very frequently a pronounced chloro-anæmia, and the patient complains of palpitation of the heart, increasing weakness, slight afternoon fever, and amenorrhœa.

(*c*) In a considerable number of cases the onset of pulmonary tuberculosis is with symptoms which suggest *malarial fever*. The patient has repeated paroxysms of chills, fevers, and sweats, which may recur with great regularity. In districts in which intermittents prevail there is no more common mistake than to confound the initial rigors of pulmonary tuberculosis with malaria.

(*d*) *Onset with Pleurisy.*—The first symptoms may be a dry pleurisy over an apex, with persistent friction murmur. In other instances the pulmonary symptoms have followed an attack of pleurisy with effusion. The exudate gradually disappears, but the cough persists and the patient becomes feverish, and gradually signs of disease at one apex become manifest. Of 90 cases of pleurisy with effusion, the history of which was followed by H. I. Bowditch, one-third developed pulmonary tuberculosis.

(*e*) *With Laryngeal Symptoms.*—The primary localization may be in the larynx, though in a majority of the instances in which huskiness and laryngeal symptoms are the first noticeable features of the disease there are doubtless foci already existing in the lung. The group of cases in which for many months throat and larynx symptoms precede the graver manifestations of pulmonary phthisis is a very important one.

(*f*) *Onset with Hæmoptysis.*—Frequently the very first symptom of the disease is a brisk hemorrhage from the lungs, following which the pulmonary symptoms may develop with great rapidity. In other cases the hæmoptysis recurs, and it may be months before the symptoms become well established. In a majority of these cases the local tuberculous lesion exists at the date of the hæmoptysis.

(*g*) *With Tuberculosis of the Cervico-axillary Glands.*—Preceding the onset of pulmonary phthisis for months, or even for years, the lymph glands of the neck or of the neck and axilla of one side may be enlarged. These cases are by no means infrequent, and they are of importance because of the latency of the pulmonary lesions. Nowadays, when operative interference is so common, it is well to bear in mind that in such patients the corresponding apex of the lung may be extensively involved.

(*h*) And, lastly, in by far the largest number of all cases the onset is with a *bronchitis* or, as the patient expresses it, a neglected cold.

There has been, perhaps, a liability to catch cold easily or the patient has been subject to naso-pharyngeal catarrh; then, following some unusual exposure, a bronchial cough develops, which may be frequent and very irritating. The examination of the lungs may reveal localized moist sounds at one apex and perhaps wheezing bronchitic râles in other parts. In a few cases the early symptoms are often suggestive of asthma with marked wheezing and diffuse piping râles.

The older writers divided the stages of pulmonary tuberculosis into *phthisis incipiens*, *phthisis confirmata*, and *phthisis desperata*, corresponding to the stages (of modern authors) of the growth and development of the tubercles, their softening, and finally the formation of cavities. While in a way useful in discussing the symptomatology of the disease, it is perhaps better to discard these stages, which are, after all, more or less arbitrary, and speak of the symptoms in detail.

Local Symptoms.—Of these cough, shortness of breath, expectoration, hæmoptysis, and pain in the side are the most prominent.

Cough.—In a few instances this important symptom may scarcely attract the attention of the patient or of the friends. In a majority of all cases it is present from the onset to the close. In the early stages it is short, dry, and hacking, without any paroxysmal quality. It may be very worrying shortly after the patient goes to bed and in the early hours of the morning. It is a cough of irritation, accompanied with only a small amount of expectoration. A very distressing form of the cough in the early stages is that which is aggravated or brought on by eating, and which is apt to be followed by vomiting. This is sometimes called Morton's cough.[1] It is occasionally a very distressing feature, and the patient may become emaciated in consequence of failure to retain sufficient nourishment. In children the cough may be paroxysmal, particularly when the tracheal and bronchial glands are greatly enlarged.

As the disease progresses to the stage of softening the cough is less irritating and is easier, being accompanied with more expectoration. While it occurs throughout the day, the early morning is still the time at which it is most marked. Sometimes with the rise of fever toward evening it becomes aggravated. In the later stages, when cavities have formed, the cough is more paroxysmal, violent, and painful. This is not, however, always the case, and in very many patients with large excavations the cough is easy and the expectoration brought up without much difficulty. At this stage position frequently has a very great influence on the cough, which may be aggravated when the patient lies on the affected side.

Cough is a feature of pulmonary tuberculosis singularly variable in its intensity. Highstrung nervous subjects are apt to be greatly troubled in all stages. The nervous element must always be taken into account, and, making use of this, Brehmer urges upon his patients most insistently the importance of *not* coughing.[2]

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[1] "Tussi phthisicae sicuti ferè semper inappentia, et sitis accedunt, ita etiàm post cibum vomitio ferè supervenire solet; adeo uti aeger à pastu continuò ferè tussire soleat, donec cibus tandèm vomitione fuerit rejectus" (*Phthisiologia*, London, 1689, p. 101).

[2] In one of the most celebrated of the *Rejected Addresses* occurs the line, "And awed consumption checks his chided cough," which would appear to indicate that the practice of Brehmer had some warrant in popular opinion.

The laryngeal complications give a peculiarly husky quality to the cough, and when erosion and ulceration have proceeded far in the vocal cords the efforts of coughing are much less effective.

Expectoration.—In the early stages, when the cough is dry, there may be no sputum, and not infrequently in a suspected case it is difficult to get sufficient for examination. Often, however, with a morning cough a little mucoid or muco-purulent matter is brought up. It may be more distinctly catarrhal, and consist of a thin, sometimes watery mucus, frothy and streaked in places with yellowish, opaque fragments. A not uncommon form in the early stage is the tenacious, gelatinous-looking sputum resembling boiled sago, and which on microscopical examination is found to be made up largely of desquamated cells of the alveolar epithelium containing myelin droplets and carbon grains. There is no distinctive character in this variety, which is met with in perfectly healthy individuals with slight bronchitic cough. In examining the sputum it should be spread on glass and the opaque yellow and greenish yellow, sharply defined streaks should be picked out to stain for bacilli and to examine for elastic tissue. As softening proceeds the sputa become more uniformly purulent, less mucoid, and frothy. The mucoid and puriform and glairy viscid varieties may occur together, though more commonly as the disease progresses the sputa become more and more purulent. Finally, in the stage of cavity formation there are expectorated rounded, flattened, greenish gray masses, which lie separated from each other in the spit-cup or at the bottom of the vessel, and which from their flattened, rounded form have been termed *nummular* sputa. When the expectoration is collected in a deep vessel these rounded masses tend to sink to the bottom. The older writers believed these *sputa globosa fundum petentia* to be a sure sign of the existence of cavities. In a typical form they certainly are most suggestive, and are rarely seen except when vomicæ are present. The color may be either of a greenish gray or of an ashy gray; the odor is often heavy and stale, rarely sweetish or fetid, except when the bronchi are dilated. In some instances, when the lung is rapidly breaking down, the sputa may be very copious and contain fragments of cheesy matter. What is called the sputum of Bayle is, I should think from his description, the form I have spoken of as resembling boiled sago or boiled rice. His original description is as follows: "Lors même que la phthisie a débuté par une toux sèche, au bout d'un certain temps il survient une expectoration muqueuse, dans laquelle on voit tantôt des filets blancs opaques, tantôt de petitis grumeaux semblables à du riz bien cuit, et quelquefois des filets de sang."[1] He is speaking of the early stages of phthisis, in which this variety is most common. I quote here Wilson Fox's remarks on this subject, as there has been some confusion about the precise character of Bayle's sputa: "Under this name are, however, included elements of the sputa having different origins. One, which is more common in the mucoid forms of expectoration, consists merely of small tenacious masses of secretion proceeding from the follicles of the throat, trachea, and bronchi, and also, I believe, in some instances from the ultimate air vesicles. They are composed of mucous and pyoid cells imbedded in a dense material of secretion. Under the same name are included small but more opaque bodies, seldom exceeding a poppy or millet seed in size, but with ragged edges and angular shape, which are necrotizing fragments of pulmonary tissue separated during the process of excavation. I have found these identical in structure in one case with the small masses often loosely attached to the interior of cavities, consisting of rapidly degenerating cells and nuclei, and having precisely the same appearances as are found in caseous tubercle." Andral states that this form of sputa was noted by Hippocrates, who compared them with grains of hail. Occasionally in cases of very rapidly softening tuberculosis quite coarse fragments of the necrotic lung tissue may be expectorated. Fibrinous casts of the bronchial tubes are occasionally expectorated in pulmonary tuberculosis.

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[1] *Réchercher sur la Phthisie pulmonaire*, G. L. Bayle, 1810, pp. 24 and 25.

Microscopical Examination.—The chief portion of the muco-purulent sputum of pulmonary tuberculosis is made up of pus cells. Epithelial cells from the mouth and pharynx and trachea and bronchi are also present in varying numbers.

Alveolar epithelial cells are present in numbers in the early stages of the disease, and their significance has been much discussed. 'The lumps of gelatinous-looking sputa which Bayle compared to boiled rice are composed almost entirely of these swollen, rounded cells, containing myelin, often carbon grains and fragments of dust. They were thought by Buhl to be distinctive of desquamative pneumonia, but they may occur in large numbers in simple bronchitis, and are quite common even in the morning expectoration of perfectly healthy individuals. I do not think their presence is of any significance whatever in tuberculosis.

Elastic Tissue.—The presence of elastic fibres in the sputum is an indication of destruction of tissue in the air passages or lungs. It is found in gangrene, abscess, and in all cases of tuberculosis with softening. For the purpose of examination it is unnecessary to resort to the tedious method of boiling the sputum with caustic potash. I have used for many years the following plan, which was shown to me at the London Hospital by Sir Andrew Clark. The method depends upon the fact that if the sputum be spread in a sufficiently thin layer fragments of the elastic tissue can be readily seen with the naked eye. . The thicker, purulent portions are placed upon a glass plate 15 by 15 cm., and flattened by a second glass plate 10 by 10 cm. In this compressed grayish layer of sputum any fragment of elastic tissue shows at once as a grayish yellow spot, and can be examined at once under a low power, or the uppermost glass is slid along until the fragment is exposed, when it is picked out and placed upon the ordinary microscopic slide. Fragments of bread, collections of milk globules, portions of epithelium of the tongue infiltrated with micrococci, also show opaquely against a black background, but with a little practice they can readily be distinguished. Every portion of elastic tissue in the sputum, even when quite small, can be readily picked out in this way. The elastic tissue from the lungs is very characteristic. The arrangement of the fibres is such that they show the outlines of the air cells. Elastic tissue from the bronchial wall forms an elongated network or two or three long narrow fibres may be seen close together. From the bloodvessels a somewhat similar arrangement of elastic tissue may be seen, or occasionally a fenestrated membrane which looks as if it had come from the intima of a good-sized ery. Elastic tissue is present in every instance of pulmonary tuber- losis with destruction. It may be found, too, very early in the disease, before the local signs of softening are at all marked.

Tubercle Bacilli.—The presence of the bacillus tuberculosis in the utum has enabled us to make the diagnosis of the disease at a much arlier period than formerly, and with an absolute certainty, even before the physical signs are in any way distinctive. While the bacilli may be resent in sputum which looks entirely glairy and mucoid, they are more kely to be found in the grayish yellow streaks of purulent sputum, hich should be picked out for the purpose of examination. They may e found sometimes in the expectoration in a case of fresh hæmoptysis a person who has had no suspicion whatever of tuberculous disease. The method has already been given for demonstrating the bacilli in sputa (p. 734).

The number of bacilli varies in different cases. Usually when softening is progressing rapidly they are very abundant, and they occur in large numbers also in the nummular sputa of old cavities.

On the other hand, there are patients who present all the local and general features of pulmonary tuberculosis, yet in whose sputa bacilli cannot be demonstrated for weeks or even for months. In other cases, again, with quite pronounced lesions for long periods, the bacilli in the sputa are very scanty. Indeed, there are cases on record in which the bacillary nature of the lung lesion has only been determined post-mortem.

Other forms of micro-organisms are frequently present in the sputum in pulmonary tuberculosis—the staphylococci, streptococci, the pneumococcus, the bacillus pyocyaneus, and the proteus. In long standing cases with cavity there may be aspergilli, sarcinæ, the leptothrix, and the oïdium albicans.

Calcareous fragments may be coughed up in chronic pulmonary tuberculosis. Formerly a good deal of stress was laid upon their presence, and Morton described a phthisis, *a calculis in pulmonibus generatis.* Bayle also described a separate form of *phthisie calculeuse.* The size of the fragments varies from a small pea to a large cherry. As a rule, a single one is coughed up; sometimes large numbers are coughed up in the course of the disease. Usually they are not associated with any special symptoms, though there are cases in which hæmoptysis has occurred. They are formed in the lung by the calcification of caseous masses, and it is said also occasionally in obstructed bronchi. They may come from the bronchial glands by ulceration into the bronchi, and there is a case on record of suffocation in a child from this cause.

Hæmoptysis.—One of the most famous of the Hippocratic axioms says, "From a spitting of blood there is a spitting of pus." A large majority of the older writers on the subject thought that the phthisis was directly due to the inflammatory or putrefactive changes caused by the hemorrhage into the lung. Morton in his interesting section, *Phthisis ab Hæmoptoe,* rather doubted this sequence. Laennec and Louis, and later in the century Traube, regarded the hæmoptysis as an evidence of existing disease of the lung. Desault, indeed, as far back as 1783 had said that instead of the term *phthisis ab hæmoptoe* the statement should be hæmoptysis from phthisis (Wilson Fox). From the accurate views of Laennec and Louis the profession was led away by Graves, and particularly by Niemeyer, who held that the blood in the air cells set up an inflammatory process, a common termination of which was caseation. Since Koch's discovery we have learned that many cases in which the physical examination is negative show, either during the period of hemorrhage or immediately after it, tubercle bacilli in the sputa, so that opinion has veered to the older view, and we now regard the appearance of hæmoptysis as an indication of existing disease. In young, apparently healthy persons cases of hæmoptysis may be divided into three groups. In the first the bleeding has come on without premonition, without overexertion or injury, and there is no family history of tuberculosis. The physical examination is negative, and the examination of the expectoration at the time of the hemorrhage and subsequently shows no tubercle bacilli. Such instances are not uncommon, and, though one may suspect strongly the presence of some focus of tuberculosis, yet the individuals may retain good health for many years and have no further trouble. Of the 386 cases of hæmoptysis noted by Ware in private practice, 62 recovered and pulmonary disease did not subsequently develop.

In a second group individuals in apparently perfect health are suddenly attacked, perhaps after a slight exertion or during some athletic exercises. The physical examination is also negative, but tubercle bacilli are found sometimes in the bloody sputa, more frequently a few days later.

In a third set of cases the individuals have been in failing health for a month or two, but the symptoms have not been urgent and perhaps not noticed by the patients. The physical examination shows the presence of well marked tuberculous disease, and there are both tubercle bacilli and elastic tissue in the sputa.

A very interesting systematic study of the subject of hæmoptysis, particularly in its relation to the question of tuberculosis, has just been completed in the Prussian army, and has been issued by Franz Stricker.[1] During the five years 1890–95 there were 900 cases admitted to the hospitals, which is a percentage of 0.045 of the strength (1,728,505). These, of course, were selected men at the healthiest periods of life. Of the cases, in 480 the hemorrhage came on without recognizable cause. Of these 417 cases, 86 per cent. were certainly or probably tuberculous. In only 221, however, was the evidence conclusive.

In a second group of 213 cases the hemorrhage came on during the military exercise, and of these 75 patients were shown to be tuberculous.

In 118 cases the hemorrhage followed certain special exercises, as in the gymnasium or in riding or in consequence of swimming. In 24 cases it developed during the exercise of the voice in singing or in giving command or in the use of wind instruments. A very interesting group is reported of 24 cases in which the hemorrhage followed trauma, either a fall or a blow upon the thorax. In 7 of these tuberculosis was positively present, and in 6 other cases there was a strong probability of its existence.

Among the conclusions which Stricker draws the following are the

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[1] *Festschrift zur 100 jährigen Stiftungsfeier des medizinisch-chirurgischen Friedrich-Wilhelms-Instituts*, Berlin, 1895.

amely, that soldiers attacked with hæmoptysis with-
cause are in at least 86.8 per cent. tuberculous. In the cases
n the hæmoptysis follows the special exercises, etc. of military
, at least 74.4 per cent. are tuberculous. In the cases which come
ing swimming or as a consequence of direct injury to the thorax
one half are not associated with tuberculosis.

noptysis occurs in from 60 to 80 per cent. of all cases of pul-
ry tuberculosis. It is more frequent in males than in females.
it may occur at all ages, and even in quite young children, yet
most common in young adults.

a majority of all cases the bleeding recurs. There are cases in
it is a special feature throughout the disease, so that a hemorrhagic
emoptysical form has been recognized. The amount of blood
ght up varies from a couple of drachms to a pint or more. In 69
ent. of 4125 cases of hæ [illegible] at the Brompton Hospital the
nt brought up was under [illegible] n ounce.

distinction may be drawn [illegible] ween the hæmoptysis early in the
ase and that which occurs in [illegible] later periods. In the former the
ding is usually slight, is apt to recur, and fatal hemorrhage is very
are. In these instances the bleeding is usually from small areas of
ftening or from early erosions in the bronchial mucosa. In the later
riods, after cavities have formed, the bleeding is, as a rule, more pro-
se and is more apt to be fatal. Single large hemorrhages, proving
ickly fatal, are very rare, except in the advanced stages of the
ease. In these cases the bleeding comes either from an erosion of a
od-sized vessel in the wall of a cavity or from the rupture of an
eurysm of the pulmonary artery.

The bleeding, as a rule, sets in suddenly. Without any warning the patient may notice a warm salt taste and the mouth fills with blood. It may come up with a slight cough. The total amount may not be more than a few drachms, and for a day or two the patient may spit up small quantities. When a large vessel is eroded or an aneurysm bursts, the amount of blood brought up is large, and in the course of a short time a pint or two may be expectorated. Fatal hemorrhage may occur into a very large cavity without any blood being coughed up. The character of the blood is, as a rule, distinctive. It is frothy, mixed with mucus, generally bright red in color, except when large amounts are expectorated, and then it may be dark. The sputa may remain blood-tinged for some days or there are brownish black streaks in the sputa, or "friable nodules consisting entirely of blood corpuscles" may be coughed up. Blood moulds of the smaller bronchi are sometimes expectorated.

The microscopical examination of the sputum in tuberculous cases is most important. If carefully spread out, there may be noted, even in an apparently pure hemorrhagic mass, little portions of mucus from which bacilli or elastic tissue may be obtained.

Dyspnœa.—In the early stages the respirations may be a little hurried, and in a few instances the dyspnœa is quite marked. When the disease is advanced, so long as the patient remains at rest there is no shortness of breath, but on attempting exercise or making any special effort the respirations are much hurried. It is remarkable how much lung tissue may be destroyed without any sense of respiratory distress so long as the patient remains quiet. Occasionally, even early in the disease, there are attacks of dyspnœa at night almost asthmatic in character. Emotion or sudden exertion may at any time cause hurried breathing. Marked dyspnœa is usually due to some intercurrent trouble, the development of a lobar pneumonia or of miliary tuberculosis, a rapidly advancing broncho-pneumonia or the development of pneumothorax.

Cyanosis is also not a common symptom in chronic pulmonary tuberculosis. It is seen most commonly under conditions which cause dyspnœa. In advanced cases with much fibroid change the dyspnœa may be cardiac, and the advancing cyanosis may also result from the gradual dilatation of the right chamber of the heart.

Pain in the chest is a very variable symptom. In some cases it is present from the outset, and the patient at the examination will place his hand accurately over the portion of the lung affected. In other instances it is absent throughout. When present it is most commonly due to pleurisy, and is situated below the clavicle, along the sternal margin, or in the scapular regions. In cases of apical tuberculosis with early involvement of the pleura the pain may be a very distressing feature. In other cases the lower thoracic zone is the seat of the chief pain, particularly on drawing a deep breath. In many instances it is only a dull, aching sensation. When such shrinkage and contraction occur, with great thickening of the pleura, the intercostal nerves may be involved, and the pains persist long after the active symptoms of the disease have disappeared. The sensitiveness to percussion may be very much increased, and the patient may wince even on light percussion over the affected area.

GENERAL SYMPTOMS.—*Fever.*—Aretæus seems to have been the first to recognize phthisis as a febrile disease. His description is most characteristic: "It is accompanied by febrile heat of a continued character, but latent, ceasing indeed at no time, but concealed during the day by the sweating and coldness of the body; for the characteristics of phthisis are that a febrile heat is lighted up which breaks out at night, but during the day lies concealed in the viscera, as is manifested by the uneasiness, loss of strength, and colliquative wasting. For had the febrile heat left the body during the day, how should not the patient have acquired flesh, strength, and comfortable feeling?"[1]

Morton, so far as I know, was the first to recognize two types of fever in pulmonary tuberculosis—the inflammatory and the putrid intermittent or hectic.[2]

To get a proper idea of the daily range of fever in any case it is necessary to take the temperature every two or three hours. The usual 8 A. M. and 8 P. M. record may be very deceptive, giving neither the maximum nor the minimum temperature of the day. It may be said at the outset that a continuous type of fever is not often seen in pulmonary tuberculosis. Except in certain instances of acute pneumonic phthisis, a twenty-four hour record, with a variation of only a degree, such as is seen not infrequently in the early stage of lobar pneumonia or of typhoid fever, is most exceptional. Much more commonly the fever remittent in character, with an afternoon exacerbation. An inter- ittent type of pyrexia, also quite common, is met with sometimes in very early stages of the disease, but is most frequent in the stage cavity. In the initial period of pulmonary tuberculosis fever is one the most important symptoms. Usually toward the afternoon the ient feels a little flushed, and the thermometer records a temperature two or two and a half degrees above the normal. The morning temperature at this time may be subnormal. In other instances, par- ularly when there is rapid invasion and consolidation of the lung sue, there is pyrexia throughout the twenty-four hours with a marked fternoon exacerbation. The fever of onset in pulmonary tuberculosis may be accompanied with chills and sweats, simulating very closely a malarial intermittent fever. In this latitude to confound early tuberculosis with malarial fever is an extremely common error. The sweating which sometimes accompanies the fever of the early stages, and which may come on in the early hours of the night, rarely has the profuse and soaking character of the sweats of the later stages. This fever of onset is often associated with two other important symptoms—a chloro-anæmia and dyspepsia. Both of these are very variable. The anæmia may be most marked. Generally speaking, the presence of fever is a good differential criterion between early tuberculosis and chlorosis, but the instances of the latter disease in which fever is a marked feature may for a time be quite puzzling.

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[1] Sydenham Society's ed., p. 310.

[2] *Phthisiologia*, p. 108.

The dyspeptic symptoms are common accompaniments of the fever, but in some instances with a daily afternoon pyrexia the tongue may be clean and the appetite and digestion good.

In the period of softening—the second stage, as it is sometimes called—the fever is more pronounced, and, when the disease is progressing, remittent in character, not reaching the normal, but with a daily exacerbation in the late afternoon or evening. At this period a temperature of 103° or 103.5° F. is common. Temperatures above 104° are rare. The daily remissions are from two to three degrees. Often in this stage the remissions may be more marked, and the temperature may fall through the morning hours to normal, or even below this point. In a few instances one sees the so-called inverse type, in which the temperature is higher in the morning hours than in the evening. In the stage of cavity the hectic type of temperature may be strongly pronounced. To get a proper idea of the diurnal range a two-hourly record is necessary. A morning and evening observation may give an entirely incorrect idea of the range. When the hectic is fully established, during a very considerable part of the twenty-four hours the patient is not only afebrile, but has a subnormal temperature. The afternoon exacerbation may reach from 103° to 105° F., and the maximum is usually reached some time between six and ten in the evening. After midnight the temperature begins to fall, and by eight o'clock is usually normal, reaching from 96.5° to 97.5° F. The fall in the morning is usually accompanied by a profuse sweat. A slow rise then takes place through the late morning and early afternoon hours. The extreme daily range may be remarkable, from eight to ten degrees being not uncommon, and there are instances on record of a diurnal range of 12 and 14.5° F. This wide variation is most commonly seen in the very late stages of the disease.

Fever is the most important prognostic symptom in pulmonary tuberculosis. With a temperature range from 101° to 103° or 104° F. the disease is surely progressing. It is most exceptional to find apyrexia associated either with the active development of tubercles or of caseation or with rapid softening. There are rare instances on record in which with a temperature at or below 99° the local signs and general symptoms indicate a progressive lesion.

The Pulse.—The heart's action is quickened in early stages in proportion to the height of the fever, in later stages bearing a closer relation to the degree of weakness. In young, excitable persons the pulse in the early stages may be very rapid, from 112 to 120, and there is great irritability of the heart, palpitation on slight exertion, and shortness of breath. There are instances in which palpitation and cardiac irritability are the most distressing symptoms of the early stage. In the high fever of rapid extension the pulse may be dicrotic. As the emaciation proceeds the superficial veins, particularly of the arms and hands, may be very prominent. In many cases of chronic phthisis the pulse is soft and full and the veins of the hands prominent. It is by no means infrequent to see pulsation in the peripheral veins, particularly those of the hands, and the capillary pulse in the nails may at times be readily seen.

Sweats.—At any stage of the disease profuse sweating may occur. In the fever of onset this may be associated with the chills, and the grouping of the rigor, fever, and perspiration may lead to the diagnosis of malarial fever. The sweats occur more frequently in the stages of softening and cavity formation. The most characteristic are the sweats which occur with the falling temperature of the early morning hours, and which may be of a drenching character and very exhausting to the patient. They may occur with great persistency and resist all treatment. As a rule, they are general over the surface, but in some instances they may be localized to the trunk. While the most profuse and distressing sweats are nocturnal, in many cases they occur at any time during the day if the patient happens to fall asleep, or they may follow the taking of food or any sudden emotional disturbance. In consequence of the profuse sweating the skin of the trunk is often covered with sudamina or a red miliary eruption. Sweats in the early stages are sometimes followed by a sense of comfort, and the patient congratulates himself that the fever is "breaking." Morton speaks of this as a *fraudulenta pax*. In a much larger proportion of cases the sweats are exhausting and excessively disagreeable.

Emaciation.—Loss of weight, one of the most obvious of the general symptoms of tuberculosis, and one from which the two most common names, phthisis and consumption, have been derived, is an early and constant feature of the disease. Next to the thermometer, the scales give us the best index to the progress of the disease.[1] In a few rare nces the disease may make rapid progress without causing great loss eight, but, as a rule, the emaciation is in a measure proportional to xtent of the local disease and its progress. It bears an important ion also to the fever, and the higher and the more persistent this is reater is the loss in weight. With moderate temperature one may ccasionally a gain in weight, but rarely with a pyrexia reaching e 101° F. Other agencies besides the fever may influence the loss weight, more particularly the dyspepsia which is so common, and the rhœa.

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[1] The wasting of a consumptive has never been described more graphically than by Sir Thomas Browne in his well known *Letter to a Friend:* "In this consumptive condition and remarkable extenuation he came to be almost half himself, and left a great part behind him which he carried not to the grave. And though that story of Duke John Ernestus Mansfield be not so easily swallowed that at his death his heart was not found to be so big as a nut, yet if the bones of a good skeleton weigh little more than twenty pounds, his inwards and flesh remaining could make no bouffage, but a light bit for the

HYSICAL SIGNS.—(*a*) *Inspection.*—The patient should be in the g posture, before a good light, and in the case of a male stripped, in emale at least the upper portions of the chest exposed. Attention uld be first given to the shape of the chest, which is often in tuberous subjects long and narrow. Both Hippocrates and Galen laid t stress upon defective conformation of the chest in phthisis, the ner describing particularly the so-called winged scapulæ. In a large portion of cases the thorax is long and narrow, with wide intercostal aces, the ribs more vertical in direction than normal, and the costal angle very narrow. Frequently the chest is flattened in an antero-posterior direction, or the costal cartilages of one or both sides may be prominent, while the sternum is depressed. Occasionally the lower sternum presents a deep cavity, the so-called funnel breast (*Trichterbrust*). The two sides of the chest may be unsymmetrical. In the early stages no difference may be noticed in the clavicular regions, but in apical disease which has lasted for any time there are changes which at once attract attention: the clavicle on the affected side is more prominent; the supra- and infraclavicular spaces are more distinct; and there may be well marked flattening corresponding to the first, second, and third ribs of this side. In very long standing cases the intercostal spaces may be much narrower and the affected side considerably shrunken. The condition of the præcordia should be carefully noted, as a wide area of impulse, particularly in the second, third, and fourth interspaces, is often associated with chronic tuberculosis of the left apex. Special attention should then be given to estimating the mobility of the two sides, noting particularly whether the apices expand equally or whether the movement on one side is retarded. Defective expansion of one apex is an early and valuable sign, particularly in women.

While marked deviations from the normal are common enough in the thoraces of persons affected with pulmonary tuberculosis, it is well to bear in mind that there are many cases in which the patients show perfectly well formed chests.

(*b*) *Palpation.*—With the hands placed beneath the clavicles one can estimate well the degree of expansion or any deficiency on either side. Standing behind the patient with the thumbs in the suprascapular and the fingers in the infraclavicular spaces, one can often judge very

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grave. I never more lively beheld the starved characters of Dante in any living face; an *aruspex* might have read a lecture upon him without exenteration, his flesh being so consumed that he might in a manner have discerned his bowels without opening of him: so that to be carried, *sextâ cervice*, to the grave, was but a civil unnecessity; and the complements of the coffin might outweigh the subject of it."

accurately the relative mobility of the two sides. The condition of the intercostal spaces, the exact position of the apex beat, the presence or absence of pain in any region, are also points to be estimated by palpation. On asking the patient to count while palpation is made at the different parts, one estimates the vocal vibrations, which are normally more forcible at the right than at the left apex, and which are much increased in all stages of tuberculous disease at the apices and over any part of the lung where consolidation has taken place. On the other hand, if a pleural exudate complicates the disease, the fremitus is greatly diminished or absent.

(c) *Percussion.*—In the early stages of pulmonary tuberculosis this method of examination gives us less valuable information than inspection or auscultation. With well marked deficient expansion at an apex there may be scarcely any change in the percussion note beneath the clavicle. In other instances the resonance is only slightly defective. In a few cases one meets with a hyperresonant note or a distinct Skodaic resonance. One of the earliest and most valuable signs is defective resonance above, upon, or below one clavicle. In a considerable proportion of all cases of phthisis the change in the note is first found in these regions. A comparison between the two sides should be made also when the breath is held after a full inspiration, as the defective resonance may then be more clearly marked. In the early stages the percussion note is usually higher in pitch, and may require an experienced ear to detect the difference. In recent consolidation from caseous pneumonia the percussion note often has a tubular or tympanitic quality. A wooden dulness is rarely heard except in old cases with extensive fibroid change at the apex or base. Over large thin-walled cavities at the apex the so-called cracked-pot sound may be obtained. In thin subjects the percussion should be carefully practised in the supraspinous fossæ and the interscapular spaces, as they correspond to very important areas early involved in the disease. In cases with numerous separated cavities at the apex, without much fibroid tissue or thickening of the pleura, the percussion note may show little change, and the contrast between the signs obtained on auscultation and percussion is most marked.

In the direct percussion of the chest, particularly in thin patients over the pectorals, one frequently sees the phenomenon known as *myoidema*, a local contraction of the muscle causing bulging, which persists for a variable period and gradually subsides. It has been thought by some to be more frequently met with in pulmonary tuberculosis than in other diseases. It has, I think, no special significance.

(*d*) *Auscultation.*—Corresponding areas on the two sides should be examined, at first during quiet respiration, then during deep breathing, and finally during the act of coughing. In very early disease of one apex the inspiration on quiet breathing may be scarcely audible; expiration is, as a rule, prolonged. On the other hand, the earliest noticeable change may be a harsh, rude inspiratory murmur. On deep breathing it is well to remember that the normal pitch is somewhat higher and the expiration somewhat more prolonged at the right than at the left side, particularly at the apex. The inspiration may be jerking or wavy, the so called cog-wheel rhythm, which is best heard when the patient draws p breath slowly. It is by no means limited to or characteristic of rculosis. With pneumonic consolidation and caseation there may luring both inspiration and expiration the most typical tubular th sounds.

Râles early accompany these changes in the respiratory murmur. y are due to the associated bronchitis. They may be only heard on o inspiration or on coughing, and very early in the disease are crack- in character—the so-called dry crackling or subcrepitant râles. On ghing they may disappear, or they may become louder and moister uality. With this there may be sometimes at the end of inspiration iping bronchial râle. As the disease progresses the adventitious sounds become louder, and what is known as the mucous or moist râle is heard, which is louder, moister, and more bubbling in character. Sometimes at the very end of inspiration these moist râles have a very clicking quality. In each instance it is important to note the quality of the râles on quiet and deep breathing and on coughing, and to observe whether they occur with both inspiration and expiration, and whether the character of the respiratory murmur is obscured or not.

When cavities form the râles are louder, more gurgling, and resonant in quality. Over an area of consolidation the breath sounds are tubular, and in the large excavations loud and cavernous or have an amphoric quality. In the unaffected portions of the lobe and in the opposite lung the breath sounds may be harsh and even puerile. The vocal resonance is usually increased in all stages of the process, and bronchophony and pectoriloquy are met with in the regions of consolidation and over cavities. Pleuritic friction may be present at any stage, and, as mentioned before, occurs very early. There are cases in which it is a marked feature throughout. When the lappet of lung over the heart is involved there may be a pleuro-pericardial friction, and when this area is consolidated there may be curious clicking râles synchronous with the heart beat, due to the compression by the heart of, and the expulsion of air from, this portion. An interesting auscultatory sign, met most commonly in phthisis, is the so-called cardio-respiratory murmur, a whiffing systolic bruit due to the propulsion of air out of the tubes by the impulse of the heart. It is best heard during inspiration and in the antero-lateral regions of the chest.

A systolic murmur is very often heard in the subclavian artery of one or other side. It has been thought to be due to compression of the artery by the apex of the lung or to pressure by a thickened pleura. It is heard best, as a rule, during expiration. It is of no moment, and occurs in thin-chested persons apart altogether from any disease of the apices.

Signs of Cavity.—In long standing cases, if the cavity is at the apex, signs of retraction in the infraclavicular region become intensified. Very pronounced unilateral retraction in this region with immobility is a sign of great value. Usually the muscles have undergone atrophy and the chest walls are thin. In very rare instances in a thin-walled cavity there is slight bulging in the first and second interspaces.

The vocal fremitus is much increased, a point of great moment in the differentiation of very large cavities from pneumothorax. The percussion sound over a cavity may be very variable. In a few instances when there is not much thickening of the pleura or induration of the surrounding lung tissue, the note may be full and clear. More commonly there is a high-pitched wooden note, which may have a tympanitic or even an amphoric quality, and which may undergo many alterations. The tympanitic quality may disappear when the cavity is full of liquid. The note may change distinctly in pitch when the mouth is opened or closed (Wintrich's sign), or alters during deep inspiration or deep expiration or with the change in the position of the patient. The cracked-pot sound—*bruit de pot fêlé*—is heard over large cavities with thin walls. To elicit it the patient should draw at first two or three deep breaths, and then breathe quietly with the open mouth. The percussion stroke should be quick and forcible. The cracked-pot sound is not distinctive of cavity. It is heard sometimes over the normal chest in childhood, over the upper portion of a lung compressed by fluid, in the early stages of pneumonia, and over the apices in some instances of acute tuberculosis, and in pneumothorax.

On auscultation over a cavity the breath sounds are heard very much altered in various grades—tubular, cavernous, or amphoric. It is important to bear in mind that the inspiratory murmur heard over cavities of medium size may be typically tubular or blowing. In larger excavations the quality of both inspiration and expiration may be what is termed cavernous, a variety of the bronchial breathing which possesses in a high degree a hollow quality very difficult to define, but readily appreciated by the ear. In very large cavities both inspiration and expiration may be typically amphoric. There may be a sharp, hissing sound, as if the air was passing from a narrow opening into a wide space. Over the entire area of a large cavity there may be dead silence (Walshe), which may be due either to complete filling with secretion or to temporary blocking of the tubes. Cavernous râles are coarse, bubbling in quality, resonant, and on coughing they may be very loud and gurgling. They are usually increased by deep inspiration or by coughing; they are not always present, and in some large cavities the breath sounds may be perfectly dry. In very large, thin-walled cavities the râles may have an amphoric echo, almost resembling that of pneumothorax. Metallic tinkling is rarely heard. In large excavations of the left apex the heart impulse may cause gurgling sounds or clicks synchronous with the systole. They may even be loud enough to be heard at a little distance from the chest wall. A large cavity with smooth walls and thin fluid contents may give the succussion sound when the trunk is abruptly shaken (Walshe), and even the *coin sound* may be obtained.

The vocal fremitus is greatly increased over a cavity. The whispering pectoriloquy is heard better than under any other circumstances, though it is not, as was supposed, pathognomonic of a cavity. In large apical cavities the heart sounds may be heard with great intensity, and there may be a loud systolic murmur, which is probably always transmitted to, and not produced in, the cavity.

COMPLICATIONS OF PULMONARY TUBERCULOSIS.—1. *In the Respiratory System.*—The larynx is rarely spared in chronic pulmonary tuberculosis. As already stated, the first symptom may be huskiness of the voice. Involvement of these parts is indicated by alterations in the character of the voice, pain, particularly in swallowing, and a cough which is often wheezing, and in the latter stages very ineffectual. phonia and dysphagia are the two most distressing symptoms of the ryngeal involvement. When the epiglottis is seriously diseased and e ulceration extends to the lateral wall of the pharynx, the pain in wallowing may be very intense, or, owing to the imperfect closure of e glottis, there may be coughing spells and regurgitation of food through the nostrils. Bronchitis and tracheitis are almost invariable accompaniments of chronic pulmonary tuberculosis. When the former extends beyond the area involved in the local disease it may increase the dyspnœa, and in the smaller tubes may lead to patchy areas of broncho-pneumonia. Extensive ulcerative tracheitis may exist without any symptoms.

Pneumonia is a not infrequent terminal complication of chronic phthisis. It may run a perfectly normal course, while in other instances resolution may be delayed, and one is in doubt, in spite of the abruptness of the onset, as to the presence of a simple or a tuberculous pneumonia.

Emphysema of the uninvolved portions of the lung is a common feature, rarely producing any special symptoms. There are, however, cases of chronic tuberculosis in which emphysema dominates the picture, and in which the condition develops slowly during a period of many years. (General subcutaneous emphysema, which has been met with in a few rare cases, is due either to perforation of the trachea or to the rupture of a cavity closely adherent to the chest wall.)

Gangrene of the lung is an occasional event in chronic pulmonary tuberculosis, due in almost all instances to sphacelus in the walls of the cavity, rarely in the lung tissue itself.

Complications in the Pleura.—As already mentioned, a dry pleurisy is a very common accompaniment of the early stages of tuberculosis. It is most frequently met with at the apices, and results from the direct involvement of the pleura over the affected portions of the lung. It is always a conservative, useful process. In some cases it is very extensive, and friction murmurs may be heard over the sides and back. The cases with dry pleurisy and adhesions are of course much less liable to the dangers of pneumothorax. Pleurisy with effusion more commonly precedes than develops in the course of pulmonary tuberculosis. Still, it is common enough to meet with cases in which a sero-fibrinous effusion develops in the course of the chronic disease. There are cases in which it is a special feature, and it often, I think, favors chronicity. A patient may during a period of four or five years have signs of local disease at one apex with recurring effusion in the same side. Owing to adhesions in different parts of the pleura the effusion may be encapsulated. Hemorrhagic effusions, which are not uncommon in connection with tuberculous pleurisy, are comparatively rare in chronic phthisis. Chyliform or milky exudates are sometimes found. Purulent effusions are not frequent apart from pneumothorax. An empyema, however, may develop in the course of the disease or as a sequence of a sero-fibrinous exudate. Pneumothorax is an extremely common complication of chronic pulmonary tuberculosis. It may occur early in the disease, but more frequently is late. It may prove fatal in twenty-four hours. In other instances a pyo-pneumothorax develops and the patient lingers for weeks or months. In a third group of cases it seems to have a beneficial effect on the course of the disease. Daland reported a case from my wards in Philadelphia in which a patient with chronic phthisis and pneumothorax was under observation for nearly four years.

2. *Symptoms referable to Other Organs.*—(*a*) *Cardio-vascular System.*—The retraction of the left upper lobe exposes a large area of the heart. In thin-chested subjects there may be pulsation in the second, third, and fourth interspaces close to the sternum. Sometimes with much retraction of the left upper lobe the heart is drawn up. A systolic murmur in the second left intercostal space, near the sternum, is common in all stages of phthisis. Apical murmurs are also not infrequent, and may be extremely rough and harsh without necessarily indicating that endocarditis is present. The association of heart disease with phthisis is not, however, very uncommon. I met with 12 instances of endocarditis in 216 autopsies. The symptoms are indefinite, and a diagnosis could rarely be made unless embolic features were present. The arterial tension is usually low in phthisis, and the capillary resistance lessened, so that the pulse is often full and soft even in the later stages of the disease. The capillary pulse is not infrequently met with, and pulsation of the veins in the back of the hand is occasionally to be seen.

(*b*) *Blood Glandular System.*—An early chloro-anæmia is a striking symptom in many cases. In the later stages the blood count rarely sinks below 2,000,000 per c.mm. The blood plates are, as a rule, enormously increased, and are seen in the withdrawn blood as the so-called Schultze's granule masses. They are of interest chiefly from the fact that every year or two some one announces their discovery as a new diagnostic sign in phthisis. The leucocytes are greatly increased, particularly in the later stages.

(*c*) *Gastro-intestinal System.*—The tongue is usually furred, but may be clean and red. Small aphthous ulcers are sometimes distressing. A red line on the gums, a symptom to which at one time much attention was paid as a special feature of phthisis, occurs in other cachectic states. Extensive tuberculous disease of the pharynx, associated with similar affection of the larynx, may interfere seriously with deglutition and prove a very distressing and intractable symptom.

Of late special attention has been paid to the gastric symptoms of this affection. Tuberculous disease of the stomach is rare. Ulceration may occur as an accidental complication, and multiple catarrhal ulcers are not uncommon. Interstitial and parenchymatous changes in the mucosa are common (possibly associated with the venous stasis) and lead to atrophy, but these cannot always be connoted with the symptoms, and they may be found when not expected. On the other hand, when the gastric symptoms have been most persistent the mucosa may show very little change. It is impossible always to refer the anorexia, nausea, and vomiting of consumption to local conditions. The hectic fever and the neurotic influences, upon which Immermann lays much stress, must be taken into account, as they play an important rôle. The stomach is often dilated, and to muscular insufficiency alone may be due some of the cases of dyspepsia. The condition of gastric secretion s not constant and the reports are discordant. In the early stages here may be hyperacidity; later, a deficiency of acid.

Anorexia is often a marked sympton at the onset; there may be ositive loathing of food, and even small quantities cause nausea. netimes without any nausea or distress after eating the feeding of patient is a daily battle. Nausea and vomiting, though occasionally roublesome at an early period, are more marked in the later stages. The latter may be caused by the severe attacks of coughing. S. H. Habershon refers to four different causes of the vomiting in phthisis: (1) central, as from tuberculous meningitis; (2) pressure on the vagi by caseous glands; (3) stimulation from the peripheral branches of the vagus, either pulmonary, pharyngeal, or gastric; and (4) mechanical causes.

Of the intestinal symptoms diarrhœa is the most serious. It may come on early, but is usually a symptom of the later stages, and is associated with ulceration, particularly of the large bowel. Extensive ulceration of the ileum may exist without any diarrhœa. The associated catarrhal condition may account in part for it; in some instances it is due to amyloid degeneration of the mucous membrane.

(*d*) *Nervous System.*—(1) *Focal symptoms* may be due to the development of coarse tubercles and areas of tuberculous meningo-encephalitis. Aphasia, for instance, may result from the growth of meningeal tubercles in the fissure of Sylvius, or even hemiplegia may develop. The solitary tubercles are more common in the chronic phthisis of children. (2) *Basilar meningitis* is an occasional complication. It may be confined to the brain, though more commonly it is a (3) *cerebro-spinal meningitis*, which may come on in persons without well developed local signs in the chest. Twice have I known strong, robust men brought into hospital with signs of cerebro-spinal meningitis in whom the existence of pulmonary disease was not discovered until the post-mortem. (4) *Peripheral neuritis*, which is not common, may cause an extensor paralysis of the arm or leg, more commonly the latter, causing foot-drop. It is usually a late manifestation. (5) *Mental Symptoms.* It was noted, even by the older writers, that consumptives had a peculiarly hopeful temperament, and the *spes phthisica* forms a curious characteristic of the disease. Patients with extensive cavities, high fever, and too weak to move will often make plans for the future and confidently expect to recover.

Apart from tuberculosis of the brain, there is sometimes in chronic phthisis a form of insanity not unlike that which develops in the convalescence from acute affections. The question of the mutual relations of insanity and phthisis is dwelt upon at length in Mickle's Goulstonian Lectures.[1]

(*e*) A remarkable *hypertrophy of the mammary gland* may occur in pulmonary tuberculosis, commonly in males. It may only be on the affected side. It is referred to in another place.

(*f*) *Genito-urinary System.*—The urine presents no special peculiarities in amount or constituents. Fever, however, has a marked influence upon it. Albumin is met with frequently, and may be associated with the fever or is the result of definite changes in the kidneys. In the latter case it is more abundant and more curdlike. Amyloid disease of the kidneys is not uncommon. Its presence is shown by albumin and tube casts in the urine, and sometimes by a great increase in the amount of the urine. In other instances there is dropsy, and the patients have all the characteristic features of chronic Bright's disease.

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[1] *Lancet*, 1888, i.

Pus in the urine may be due to disease of the bladder or of the pelves of the kidneys. In some instances the entire urinary tract is involved. In pulmonary phthisis, however, extensive tuberculous disease is rarely found in the urinary organs. Bacilli may be detected in the pus. Hæmaturia is not a very common symptom. It may occur occasionally as a result of congestion of the kidneys, which passes off and leaves the urine albuminous. In other instances it results from disease of the pelvis or of the bladder, and is associated either with early tuberculosis of the mucous membranes or more commonly with ulceration. In any medical clinic the routine inspection of the testes for tubercle will save two or three mistakes a year.

(*g*) *Cutaneous System.*—The skin is often dry and harsh. Local tubercles occasionally develop on the hands. There may be pigmentary staining, the *chloasma phthisicorum*, which is more common when the peritoneum is involved. Upon the chest and back the brown stains of the *pityriasis versicolor* are very frequent. The hair of the head and beard may become dry and lanky. The terminal phalanges, in chronic cases, become clubbed and the nails incurvated—the Hippocratic fingers.

DIAGNOSIS.—When well advanced there is rarely any doubt as to existence of tuberculous phthisis, for the sputum gives positive information and the physical signs of local disease are well marked. The bacilli give an infallible indication of the existence of tuberculosis, and may be found in the sputum before the physical signs are at all definite. On the other hand, it must be remembered that there are cases in which, even with tolerably well defined physical signs, the sputum is extremely scanty, and many examinations may be required to detect tubercle bacilli. *Early detection is of vital importance, as successful treatment depends upon the measures taken before the lungs are extensively involved.*

The presence of elastic fibres in the sputum is an indication of destruction of the lung tissue. In a large proportion of cases it is indicative too of tuberculous disease. It also may be found early, before the physical signs are well marked. Its detection is easy by the above mentioned method, not requiring high powers of the microscope. In cases of early hæmoptysis, before there is marked constitutional disturbance or even local signs, it is very important to make a thorough examination of the sputum, from which mucoid and purulent portions may be picked out for examination. With localized and persistent signs in one lung, cough, fever, and loss of flesh, the diagnosis is rarely dubious. It is remarkable, however, to what extent the local process may sometimes proceed without disturbance of health sufficient to excite the alarm of the physician or friends. There are puzzling cases with localized physical signs at one apex, chiefly moist râles, rarely any percussion changes, perhaps slight fever, and a glairy expectoration containing numerous alveolar cells. I have seen several cases of this kind which have been for a time very obscure, and in which repeated examinations failed to detect either bacilli or elastic tissue. They seem to be instances of localized catarrh of the smaller tubes.

III. FIBROID PHTHISIS.

As already mentioned, sclerosis is in some degree a constant accompaniment of tuberculosis. There are cases in which this process dominates the picture from the very outset. Fibroid phthisis may follow a chronic tuberculous pleurisy or it may supervene upon an ordinary ulcerative tuberculosis. All grades are met with between cases which resemble, in almost every respect, the non-bacillary cirrhosis of the lung and instances of ulcerative tuberculosis with cavity formation and extensive shrinkage from associated sclerosis. Every case of arrested pulmonary tuberculosis is an epitome of fibroid phthisis. In the process of healing which goes on in a section of the apex the fibroid transformation, the pigmentation, and the dilatation of the bronchi form a miniature picture of what may go on in an entire lobe or in an entire lung.

MORBID ANATOMY.—So shrunken may be the lung that no trace of any natural appearance of the organ is seen. In the case of a physician who had been for twenty-five years under the observation of Palmer Howard, and who had left instructions that his lungs should be sent to the museum at McGill College, the medical men who performed the autopsy sent one enormously hypertrophied lung, and stated that the other could not be found, as it was shrivelled to a jelly-like substance. The pleural layers are enormously thickened, and it is only with the greatest difficulty that the parts can be separated from the chest wall. The entire mass of the lung may not be much larger than a spleen. In other instances the process may be confined chiefly to the upper lobe or to the upper and middle lobes. On section there may be no evidence whatever of lobes. The pleura is from 1 to 3 cm. in thickness. The normal parenchyma of the lung may be everywhere substituted by fibrous tissue. In cases which have originated in the pleura bands may be seen passing into the substance from the thickened membranes. At the apex, sometimes throughout the entire lung, there are old puckered, thick-walled cavities, some of which represent greatly dilated bronchi; others are in communication with them. About the cavities and throughout the fibrous tissue there is much pigmentation, which gives a marbled appearance to the section. Encapsulated cheesy or calcareous nodules may be present. This picture of the advanced grade of chronic fibroid tuberculosis, in which the whole lung is involved, is hardly to be distinguished from non-tuberculous cirrhosis of the lung, but in the former bacilli will be found in the walls of the cavities, and cheesy or calcareous masses are present. Even more typical are those cases in which the process is confined for a long period of years to the upper portion of the lung. The shrinkage then is remarkable, and an entire upper lobe may form a mass not half the size of the fist, shrunken, puckered, and composed of dense, deeply pigmented connective tissue, with contracted, thick-walled cavities and dilated bronchi. In such instances the lower lobe usually is the seat of chronic tuberculosis with cavities and old, hard tubercles and encapsulated cheesy and calcareous masses. The unaffected lung is usually very voluminous and emphysematous. It may present local signs of tuberculosis at the apex, or fresh tuberculosis which has proved fatal. The heart is usually enlarged, particularly the right ventricle.

CLINICAL HISTORY.—The onset and early features are in a majority of cases those of chronic ulcerative phthisis, and for a year or more the patient may present all the features of that form. After variations in the course all activity in the process subsides and the case enters upon the chronic stage. The following is a good description given by Clark, Hadley, and Chaplin:[1]

"The temperature, which before was always raised in the evening, is now often normal; the sweating becomes less and the patient regains much of his wonted strength and flesh. If one keeps the case under observation all this time, it will be seen that the affected side becomes more and more flattened, the rib spaces fall in, and the movement becomes appreciably diminished; at the same time the impairment of note becomes increasingly marked, until absolute dulness, extending over a great part of the lung, can be made out. The displacement of organs now makes its appearance. The heart is drawn toward the affected side; the stomach may be drawn up if the disease is left-sided. The lung least diseased becomes affected with compensatory hypertrophy or with emphysema, and extends across the sternum to the most diseased side. If the heart be now examined, often some hypertrophy can be made out and the beats of the organ are much altered; instead of being quick and frequent, they are slow, measured, and infrequent. The sounds heard over the diseased lung also become gradually altered. In the place of the sharp, fine, moist crepitations which could be noticed when the case was first seen, there are now coarse bubbling râles, rhonchi, and fine superficial rustling crepitations. The bronchial breathing and bronchophony are intense, and often pectoriloquy can be heard. The fingers may become much clubbed, and sometimes the urine becomes albuminous. Even the countenance can sometimes be observed to wear a congested appearance. The dyspnœa remains very much what it was at first, but the cough and expectoration undergo a change. The cough is now paroxysmal, often bad in the morning on waking, and attended with gushes of expectoration, which suggest the emptying of dilated tubes. After lasting some time in this condition the patient generally succumbs to a fresh eruption of tubercles in the least affected lung or to an attack of hæmoptysis. Owing to the altered condition of the bloodvessels, and especially to their diminished elasticity, hæmoptysis is sometimes more prolonged and severe in these cases than in cases of ordinary tuberculosis."

The clinical course of tuberculo-fibroid disease of the lung is extremely varied. There are instances in which after a year or two the patient has little or no further trouble, and he would consider himself quite well except for the morning cough with a slight amount of expectoration. In other cases there are periodical slight rises in temperature with aggravation of the cough, and for years there may be alternations of these outbreaks with prolonged periods of quiescence. Recurring hemorrhages form a very striking feature in some of the cases.

An important change proceeds in the condition of the heart and arteries. In consequence of the gradual obliteration of a large area of the pulmonary circulation there is hypertrophy of the right heart, and the area of cardiac pulsation is usually extensive. The peripheral arteries become gradually sclerotic, and there may be well marked phlebosclerosis. Three dangers threaten cases of fibroid tuberculous disease: (1) hemorrhage, which is usually profuse, and comes either from an eroded vessel in the wall of the cavity or from the rupture of a small aneurysm; (2) extension or generalization of the tuberculosis; (3) failure of the hypertrophied heart. Of these the last is perhaps the most important. A certain number of patients succumb with gradual dilatation of the right heart and anasarca. There are instances in which this has been combined with amyloid disease of the kidney—not, in my experience, a very common sequel of the disease. There are other instances in which there is more acute dilatation of the heart and the patient dies with urgent orthopnœa and cyanosis.

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[1] *On Fibroid Phthisis*, London, 1894.

Diagnosis.—It is not, as a rule, difficult to distinguish cases of tuberculo-fibroid disease from cirrhosis of the lung due to other causes. The history is of importance, as the latter disease usually follows a pleurisy, a pneumonia, a broncho-pneumonia, or a prolonged bronchitis, so that the mode of onset and preliminary features are very different in the two conditions. Once established, cirrhosis of the lung is very much less liable to be interrupted by febrile outbreaks and the general health and vigor are of a very much higher standard. In the monograph just referred to the authors very justly lay considerable stress upon the very different aspect of the patients: "A case of tuberculo-fibroid disease, however fibroid it may become, always bears, in the general aspect of the patient, evidence of its tubercular origin. The cast of countenance is not of that heavy kind so often observable in the pure fibroid variety. The lips are not thick and congested, the complexion has not the muddy look, the hair remains lank, and the eyelashes long. The whole appearance of the face suggests tubercle and frail health. It is true that one does meet with tuberculo-fibroid disease in which the fibroid characters are somewhat clearly marked in the face, but never, so far as we are aware, to the extent of its being mistaken for pure fibroid disease."

The presence of tubercle bacilli is a very important point in the diagnosis. It is surprising, indeed, how they persist in long standing cases in which the symptoms have been quiescent for years. When not evident during life the tuberculous character of the lesions may be determined sometimes post-mortem by the presence of encapsulated caseous masses.

Chronic syphilis of the lung occasionally produces conditions which may simulate this form of pulmonary tuberculosis. The special points which would favor the former are the pronounced history of syphilis, the coexistence of syphilitic lesions, the chronic course, often with very slight or no fever. The local signs are more commonly in the middle regions of the lungs toward the root, and are associated with chronic fibroid changes. The dulness may be very wooden in quality and clearly defined. The apex of the lung is often spared. The most important of all is the existence of a chronic lesion of the lung in a syphilitic person without tubercle bacilli in the expectoration. It sometimes happens that a syphilitic lung becomes infected with tuberculosis.

Concurrent Infections in Pulmonary Tuberculosis.—The complex anatomical and clinical picture of pulmonary tuberculosis is not the outcome of the action of the bacillus tuberculosis alone. It is well known that other organisms play an important rôle. The observations of Babes, Cornet, Ortner, and others have shown the very frequent association of the micrococcus lanceolatus, the streptococcus pyogenes, the staphylococcus aureus, and the bacillus pyocyaneus. Their work has been confirmed by many subsequent observers, and in the stage of hectic the pyogenic organisms have even been isolated from the blood.

Prudden, who has very carefully studied this question, arrives at the following conclusions: The pulmonary lesions of tuberculosis are subject to variations depending largely on the different modes of distribution of the bacilli, whether by the bloodvessels or through the bronchi, and also whether a concurrent infection with other organisms has taken place. The pneumonia complicating tuberculosis may be the direct result of the tubercle bacillus or its toxins, or it may follow secondary infection with other germs, particularly the streptococcus pyogenes, the micrococcus lanceolatus, and the staphylococcus pyogenes. The frequency of this secondary infection and the relative significance of these germs are not yet fully decided. The introduction of the tubercle bacilli into the lungs of a rabbit through the trachea induces the various phases of pulmonary tuberculosis, but cavity formation is rare. If, on the other hand, into the lungs of a rabbit which are the seat of extensive consolidation the streptococcus pyogenes is introduced, then cavities form rapidly, and the anatomical picture is very similar to that of chronic ulcerative tuberculosis in man. It is very probable that in man, too, the effect of contamination with these pus organisms is a very important one in hastening necrosis and softening, and also in the chronic cases they doubtless produce in large amounts the toxins which are responsible for many of the symptoms of the disease.

DISEASES ASSOCIATED WITH PULMONARY TUBERCULOSIS.—*Lobar pneumonia*, as already mentioned, is a not uncommon complication which carries off a certain number of cases. It may be difficult to distinguish from an acute tuberculous pneumonia. In chronic ulcerative tuberculosis, however, this form is not so common, and rapid consolidation of the lower lobe, with rusty expectoration and high fever, is much more likely to be a simple croupous pneumonia. With tuberculosis, either in the acute or chronic form, *typhoid fever* may coexist. In 4 cases of 80 autopsies in typhoid fever tuberculous lesions were present. There are cases on record also of acute miliary tuberculosis and typhoid fever present in the same subject. There is a widespread opinion that typhoid fever predisposes to tuberculosis, and Wilson Fox in his treatise on diseases of the lungs gives references to a number of cases. In my experience it has been very rare. I have no recollection of an instance in which tuberculosis has developed either during convalescence, or immediately after recovery, from typhoid fever.

Erysipelas sometimes attacks the subjects of chronic phthisis, who are not, however, specially liable to the disease. There are a number of cases on record in which an attack of erysipelas has been beneficial, and after recovery the severity of the pulmonary symptoms has mitigated, and there are cases in which cure has been reported. On the other hand, I have known cases in which the attack has proved rapidly fatal in persons far advanced in the disease.

The *eruptive fevers* rarely develop in the course of pulmonary tuberculosis. Malaria was formerly thought to antagonize tuberculosis, a view for which there is no special warrant. The early chills and fever of developing pulmonary tuberculosis are very apt to lead to error in diagnosis, and cases are often treated for weeks or months as malarial intermittent fever.

Heart Diseases.—Endocarditis is not very infrequent in pulmonary tuberculosis. It was present, as already mentioned, in 12 of my post-mortems and in 27 of Percy Kidd's 500 autopsies. The subject has been considered in a monograph by Teissier (Paris, 1894). The endocardial lesions are, as a rule, vegetative, rarely caseous, and due commonly to the associated micro-organisms, but in a few instances the tubercle bacillus has been present alone. Ulcerative lesions are rare. Both Louis and Rokitansky held that there was a certain antagonism between valvular disease and pulmonary tuberculosis—a view which has not been borne out by subsequent studies. Certainly stenosis of the pulmonary artery and aneurysm of the aorta predispose to tuberculosis pulmonum. A terminal acute tuberculosis is a common event in all forms of cardio-vascular disease. The relation of mitral stenosis to pulmonary tuberculosis is still a matter of debate. In 9 of 54 cases of stenosis Potain found pulmonary tuberculosis present. Teissier concludes that it is antagonistic to the progress of the disease. In long standing cases of the disease arterio-sclerosis is very common. Phlebo-sclerosis is also not infrequently met with. The frequency of the renal changes may possibly be correlated with this arterio-sclerosis. Ormerod noted 30 cases of chronic renal disease in 100 autopsies.

The association of gout and rheumatism with pulmonary tuberculosis has often been referred to, particularly by the older writers, among whom Morton described a species—*phthisis de arthritide.* In institution life, particularly in the almshouses, the subjects of chronic joint troubles are very often attacked by tuberculosis, and it is probably a matter entirely of greater liability to infection.

PECULIARITIES OF PULMONARY TUBERCULOSIS AT THE EXTREMES OF LIFE.—(*a*) *Infancy.*—Tuberculosis is a widespread affection in the early periods of life. While extremely rare in the newborn, and not at all prevalent in the first three months of life, the cases increase rapidly throughout the latter half of the first year and during the second year. In the statistics of the late Professor Parrot, of 219 cases in children under three years there were from one day to three months 23 cases; from three to six months, 35 cases; from six to twelve months, 53 cases—a total of 111 cases under one year. Pulmonary cavities were present in 57 of the cases, and in 50 the lung disease was the only manifestation. Of 125 cases at the New York Foundling Hospital, reported by Northrup, in 34 cases the disease was extensive and the seat of the primary infection was not clear, but the bronchial glands were large and cheesy. In 42 cases of general tuberculosis the only caseous masses were in the bronchial glands. In 9 cases the tubercles were limited to these glands and to the lungs, the latter containing only miliary tubercles, while the bronchial glands were in a state of advanced caseation. In 13 cases there was tuberculosis of the bronchial glands only. These extremely suggestive figures show the great prevalence of infection through the bronchial passages. On the other hand, of 127 fatal cases of tuberculosis in children noted by Woodhead, the mesenteric glands were tuberculous in 100. Walter Carr in the examination of the bodies of 120 tuberculous children concludes that the disease starts much more frequently in the thoracic than in the mesenteric glands. Of 500 autopsies in children at the Munich Pathological Institute, in 150 tuberculosis was present, and in over 92 per cent. of these the lungs were involved.

(*b*) *Old Age.*—The prevalence of tuberculosis in the aged, particularly in institutions, has been long known. The physicians to the large hospitals for old people, as at the Chelsea, the Bicêtre, and the Salpêtrière, have long recognized the great frequency of tuberculosis as a cause of death. In the post-mortem room of the Philadelphia Hospital, to which the bodies of aged persons were sent from the almshouse department, it was extremely common to find old or recent tuberculosis. An important study of the subject has been made recently by Barié.[1] In the year 1891 there were in Paris 10,649 deaths from pulmonary tuberculosis. In 641 of these the individuals were above the age of sixty. In the decennial period 1884 to 1893 there died of pulmonary tuberculosis in the ten large hospitals or almshouses of Paris 2202 persons between the ages of sixty and ninety-two. Among the special peculiarities of the pulmonary tuberculosis of the aged is its latency and slow course. In very many instances there are found only puckered cicatrices at the apices or calcified masses or fibroid areas. In other instances there is extensive bronchiectasis with senile emphysema, with which form and tuberculosis there is no antagonism, as believed by Rokitansky. The more acute forms of the disease are also met with, and Barié gives a number of cases of the acute pneumonic as well as the acute miliary forms of tuberculosis.

MODES OF DEATH IN PULMONARY TUBERCULOSIS.—(*a*) *By Asthenia.*—In a majority of the cases the patient sinks gradually, with progressive failure of the strength in a septicæmia. As a rule, the end is quiet and undisturbed. Consciousness may be retained until the close.

(*b*) *By Asphyxia.*—This is rarely met with apart from the development of an acute miliary tuberculosis or a rapid, widespread bronchitis of the smaller tubes.

(*c*) *By Syncope.*—This is not very common, but patients in the advanced stages of the disease during sudden exertion or while on a journey may drop dead. It will be remembered that Branwell Brontë insisted upon keeping up, and died standing.

(*d*) *From Hemorrhage.*—The fatal bleeding in chronic phthisis may come from the lungs or from the intestine. Rupture of an aneurysm in the walls of a cavity or erosion of a large vessel is the common cause of the fatal hæmoptysis. The importance of this lesion may be judged from the fact that in 35 cases collected by Percy Kidd aneurysm was present in 30. In the case of very large cavities the bleeding may prove fatal before any hæmoptysis occurs. In the body of a man very far advanced in phthisis, who died quite suddenly in the Philadelphia Hospital, I found a very large cavity, occupying almost the upper two thirds of the lung, which was filled with blood which had come from an eroded vessel in the wall of a small cavity in the lower lobe. The patient had not had hæmoptysis. Severe and fatal hemorrhage may follow ulceration of the colon, less frequently of the ileum. On several occasions I have known death to occur in chronic pulmonary tuberculosis from this cause.

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[1] *Revue de Médecine*, October, 1895.

(*e*) *With Cerebral Symptoms.*—The tuberculous meningitis may cause coma or convulsions. Uræmia as a cause of death is rare. Occasionally in very lingering cases a sudden coma may be due to thrombosis in the cerebral sinuses.

V. TUBERCULOSIS OF THE ALIMENTARY SYSTEM.

Tuberculosis of the Alimentary Canal.

(*a*) *Lips.*—Tuberculosis of the lips is very rare. It occurs occasionally in the form of an ulcer, either alone or more commonly in association with laryngeal or pulmonary disease. The process may result from extension of a focus of ulceration in the mouth, as in a case reported by Lord in 1892. In addition to a tuberculous ulceration of the right tonsil, the patient presented a small irregular ulcer on the inside of the left cheek. This gradually extended, until eighteen months later it involved both lips, which became very much swollen. A report of two cases and an analysis of the literature is given in tome iii. of Verneuil's *Études*. The ulcer is usually very sensitive, and, owing to the comparative frequency of epithelioma and of chancre of the lip, may be mistaken for these. The diagnosis in doubtful cases may be made by inoculation experiments or the examination of a portion for tubercle bacilli.

(*b*) *Tongue.*—In 1858, Sir James Paget gave a description of tuberculous ulceration of the tongue, and he is credited with having been the first to recognize this condition. Mr. Arthur Barker[1] reviewed the subject and gave an analysis of 15 cases. The disease is nearly always associated with tuberculosis of some other organ. It occurs most commonly on the dorsum or edge, although the tip is quite frequently involved. When it is associated with tuberculosis of the larynx or lungs the ulceration is usually found on the same side as the most advanced lesions in these parts. The organ may be involved by direct extension of a tuberculous ulcer of the pharynx or epiglottis, in which case the posterior portion will be first attacked. The condition is found much more commonly in males than in females. Of the 15 cases collected by Barker, 11 were in males and 4 in females. In the earliest stages an aggregation of small tubercles appears beneath the mucous membrane. The epithelium is finally shed and a point of superficial ulceration remains. By the coalescence of these small areas a definite ulcer is formed, which is characterized by having an irregular outline, distinct, uneven margin, and a rough base covered with a grayish caseous detritus. The disease extends slowly, rarely if ever heals, and may form an ulcer of considerable size. In long standing cases the base of the ulcer becomes indurated and the condition may be mistaken for epithelioma. Until the disease becomes very far advanced but little inconvenience is occasioned beyond a slight increase in the secretion of saliva. Unlike epithelioma, very little pain is complained of, and the movements of the tongue are not impeded until the late stages. In two cases of tuberculous ulceration of the tongue reported by Frerichs the submaxillary lymph glands were enlarged and caseated in both instances. From syphilitic ulceration the condition would be recognized by the history of the case and the absence of any improvement under treatment with iodide of potassium. In doubtful cases inoculation tests should be made or a portion excised for microscopical examination.

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[1] *Trans. Path. Soc., Lon.*, xxxv., 1884.

(c) *Palate.*—Tuberculosis of the hard and soft palate nearly always results from an extension of the disease from neighboring parts. Barker records a case in a girl of fifteen years in whom there had been such an extensive destruction of the hard and soft palate and the alveolar process that many of the teeth had become loosened and several had fallen out. The disease had extended into the nasal cavity.

(d) The *salivary glands* belong to that small group of organs of the body which seem to possess an immunity against tuberculous infection —an immunity, however, which in their case is relative, not absolute. The literature contains only a very few accounts of such a condition. Von Stubenrauch,[1] in reporting a case of tuberculosis of the parotid gland had been unable to find records of a previous case after a careful search of the literature. Frerichs, however, had previously recorded an instance in which both parotid glands contained four or five caseous foci, each about the size of a lentil. The submaxillary and sublingual glands were normal, although the patient presented advanced tuberculous lesions in various organs of the body. Leguen and Marien have recently reported a case resembling that of Stubenrauch, in both of which the gland presented a distinct localized swelling, the skin remaining normal in appearance and freely movable over it. The tubercles develop in the interacinous connective tissue, and the writers agree in considering that infection occurs by way of Steno's duct. Dmochowski claims to have found the sublingual gland tuberculous in 6 instances out of 15 autopsies on patients with pulmonary tuberculosis.

(e) The *tonsil* has in recent years been shown to be much more commonly the seat of tuberculosis than was formerly supposed. The apparent infrequency no doubt was due to the fact that in many instances the disease simulates very closely the ordinary hypertrophied tonsil, for which it is often mistaken. Cohnheim in 1878 advanced the theory that the majority of the cases of tuberculosis of the lips, buccal mucous membrane, and pharynx were surface infections due to the ingestion of food, particularly milk, containing tubercle bacilli. In 1884, Strassmann, working under Cohnheim and Weigert, found the tonsils involved in 13 instances out of 21 autopsies. Dmochowski found them tuberculous in all of his 15 cases, and demonstrated tubercle bacilli in the lymphatics between the tonsils and the cervical lymph glands. The latter observation is interesting in connection with the views of Schlenker,[2] who claims that the majority of the cases of tuberculous cervical glands result from

[1] *Archiv für Chirurgie*, 1894.

[2] *Virchow's Archiv*, 1893, Bd. cxxxiv.

infection with tubercle bacilli which gain admission by way of the tonsil. A large number of his cases of tuberculous cervical adenitis were definitely of a descending variety and associated with tuberculosis of these glands. The majority also had pulmonary tuberculosis, and he regards surface infection of the tonsil by tuberculous food and sputum far more common than infection by way of the circulation. The disease may occur as a superficial ulceration. More commonly there is an infiltration of the tonsil with miliary tubercles, which produces a greater or less hypertrophy which it is practically impossible to distinguish from an ordinary enlarged tonsil without a microscopical examination. Caseous foci occasionally develop.

(*f*) *Pharynx.*—In extensive laryngeal tuberculosis an eruption of miliary tubercles on the posterior pharyngeal wall is not uncommon. In chronic phthisis an ulcerative pharyngitis, due to the extension of the disease from the epiglottis and larynx, is one of the most distressing of complications and renders deglutition extremely painful and difficult. Adenoids of the nasopharynx may be tuberculous, as shown by Lermoyez. Macroscopically, they do not differ from the ordinary vegetations found in this situation. He records a case in which pulmonary tuberculosis set in soon after the removal of adenoid vegetations which were shown to be tuberculous, and thinks that in such instances the tuberculous focus in the adenoids may be the point of departure of general infection. Verneuil points out the risk of infection which is run in curettement of ordinary pharyngeal vegetations, especially since Straus has demonstrated the frequency of tuberculosis in the nasal cavities of men.

(*g*) *The Œsophagus.*—Tuberculosis of the œsophagus is a comparatively rare occurrence. It is only since the appearance of Weichselbaum's and Beck's articles in 1884 that this affection of the œsophagus has attracted attention. In 1893, Flexner, in reporting a case which occurred in my wards, was able to find in the literature records of only 19 well authenticated cases. Frerichs examined 30 cases of acute and 250 cases of chronic tuberculosis. Of the acute cases, 8 had tuberculosis of the pharynx, tonsils, or tongue without any involvement of the œsophagus. Of the chronic cases, only 1 case of œsophageal tuberculosis occurred. The cases may be classed under three headings: The first includes those which result from direct extension of the tuberculous process from some of the neighboring structures, and constitutes the largest percentage of the cases. A group of caseous bronchial glands may become united by adhesions to the œsophagus, and finally ulcerate through into the latter. Penzolt has reported 3 cases of œsophageal tuberculosis resulting from the rupture into it of abscesses due to caries of the vertebræ. Slight ulceration of the upper part of the œsophagus following pharyngeal tuberculosis occasionally occurs. The second class of cases embraces those instances in which there is a history of a previous lesion of the œsophageal mucous membrane, and which must be considered as a predisposing factor to tuberculous infection. Breus records a case in which tuberculosis of the œsophagus followed a stricture due to the swallowing of a caustic alkali, and Eppinger an instance in which it followed a stricture which he attributed to the oïdium albicans. Finally, in the third class must be placed those cases which occur in the course of an acute disseminated miliary tuberculosis, and those instances in which there has apparently been an infection of the mucous membrane with tuberculous sputum, without the presence of any previous predisposing lesion. The case which occurred in my wards belonged to this class. On the anterior wall of the œsophagus there were two tuberculous ulcers, measuring 4 and 7.5 mm. respectively, one of which had perforated into the left pleural cavity, causing a purulent pleurisy.

The disease is not associated with any very definite symptoms. The occurrence of pain, difficulty in swallowing, and evidence of stricture in the course of chronic lung and lymph tuberculosis or caries of the vertebræ should lead one to suspect involvement of the œsophagus.

(*h*) *Stomach.*—Miliary tubercles in the wall of the stomach are not uncommon; tuberculous ulcers of the organ are very rare. Many of the reported cases are doubtful. Marfan[1] in 1887 in reviewing the subject was able to collect only 14 authentic cases. Letorey[2] quite recently reported a case and gave an analysis of 21 cases. Nearly all writers are agreed that the disease is secondary. It is commonest in the middle period of life, although occasionally children are affected. The condition is found more frequently in males than in females. Of 19 cases collected by Letorey in which the sex was mentioned, it occurred 16 times in males and 3 times in females. In the great majority of instances the ulcers are single, although occasionally they may be multiple. In a recent case in one of my wards there were numerous ulcers of various sizes. As a rule, the ulcers are associated with tuberculous ulceration of the intestines. Litten, however, has reported 1 case and Frerichs has noted 2 instances in which the stomach was the only part of the alimentary tract which showed ulceration. The pyloric extremity and the greater curvature are usually involved. The ulcers vary in size from a pin's head to 3 or 5 cm. in diameter. In the case reported by Musser, however, there was a large tuberculous ulcer three by one and a half inches in extent. Cheesy tubercles as large as a pea, both ulcerated and non-ulcerated, have been found in the stomach, but they are very rare. In Oppolzer's case an ulcer of the colon perforated the organ. Perforation of the stomach is not an infrequent occurrence. It occurred six times in Marfan's cases, three times by a tuberculous gland. As a rule, the condition is latent; in 8 of Letorey's cases the ulceration was suspected during life and was verified at autopsy. Occasionally severe hæmatemesis follows erosion of a bloodvessel by the ulcerative process. It has been the immediate cause of death in at least 2 instances. Death sometimes results from a peritonitis occasioned by the perforation, as in Paulicky's case, although it generally occurs as a result of advanced tuberculosis in other organs.

(*i*) *Intestines.*—Tuberculosis is by far the most common cause of intestinal ulceration. No part of the intestinal tract enjoys an immunity against tuberculous infection. The disease may be (1) primary in the mucous membrane, or more commonly (2) secondary to disease of the lungs, or in rare cases the affection may (3) extend from the peritoneum.

(1) *Primary intestinal tuberculosis* occurs most frequently in children in association with enlargement and caseation of the mesenteric glands

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[1] *Paris Thesis*, 1887.

[2] *Ibid.*, 1895.

or with peritonitis, or with both. It may be very difficult to state at the time of the autopsy, with any degree of certainty, whether the primary lesion has been intestinal or peritoneal. The very great frequency of infection through the bowel is shown in Woodhead's analysis of 127 cases of fatal tuberculosis in children, 100 of which showed involvement of the mesenteric glands. Primary tuberculosis in adults is very rare, occurring in but 1 instance in 1000 autopsies upon tuberculous subjects at the Munich Pathological Institute. Occasionally cases occur in which the disease sets in with irregular diarrhœa, moderate fever, and colicky pains. In a few instances hemorrhage has been the initial symptom. The cases at first are apt to be regarded as chronic intestinal catarrh, and it is not until the patient becomes markedly emaciated or that signs of disease in the lungs appear that the true nature of the disease becomes apparent. More deceptive still are the cases in which the tuberculous process begins in the cæcum with symptoms suggestive of appendicitis—tenderness in the right iliac fossa, constipation, or an irregular diarrhœa and fever. Owing to the fact that in certain instances there may be a temporary alleviation of symptoms, with a recurrence at a later period, the diagnosis may be further complicated. In several of my cases death has been occasioned by hemorrhage. Perforation may occur with the formation of pericæcal abscess, or in less fortunate cases perforation into the peritoneal cavity may occur, causing death from general peritonitis. In rare instances there is partial healing of the ulcer, with great thickening of the walls and narrowing of the lumen of the bowel.

(2) *Secondary tuberculosis of the bowel* is very common in chronic pulmonary tuberculosis. It was present in 566 of the 1000 Munich autopsies in tuberculosis already referred to. Only 3 of these cases failed to show involvement of the lungs. In Frerichs' series of 250 cases of chronic tuberculosis the intestines showed tuberculous ulceration in 83 per cent. of the cases. The lesions are found chiefly in the lower part of the ileum, in the cæcum, and in the colon. Frerichs found the ileum involved in 200, the colon in 115, and the rectum in 18 cases. The colon was alone diseased in 8 instances. There was extensive ulceration of the duodenum in 1 case, which also showed tuberculous ulceration of the stomach. In a second instance the duodenal mucous membrane presented several tuberculous ulcers closely set together near the pyloric orifice. In this latter instance the stomach was free from ulceration, and the remainder of the small intestines was healthy, but the colon showed extensive tuberculous ulceration. The disease begins with an eruption of miliary tubercles in the solitary or agminated glands or on the surface of or within the mucous membrane. In the solitary follicles, owing to caseation and necrosis of the tubercles, a loss of substance is produced, with the production of a crater-like ulceration. In the case of Peyer's patches all the individual follicles are not simultaneously attacked, so that their surfaces are irregular, a portion having undergone destruction by ulceration, whilst in the early stages islands of the normal gland still remain. This differs from the ulceration found in Peyer's patches in typhoid, where the destruction is much more uniform throughout the surface of the gland. The edges of the ulcers are thickened and infiltrated with tubercles which are constantly undergoing caseation and necrosis, thus producing a more or less wormeaten

appearance and irregular outline to the ulcers. In the ileum, in which Peyer's patches are chiefly involved, the ulcers may be ovoid. In the jejunum and colon they may be round, but one of the characteristic features of the intestinal tuberculous ulcer is its tendency to increase in size in a direction at right angles to the long axis of the intestine, so that ulcers are finally formed which entirely encircle the bowel, the so-called girdle ulcer. This direction of spreading is due to the fresh tubercles developing along the lines of the bloodvessels and lymphatics, which run transversely to the long axis of the intestine. Such ulcers may be simulated by embolic ulcers due to the plugging of a vessel supplying a portion of the mucous membrane with nourishment, but would be distinguished by the presence of tubercles about the edges and on the base of the ulcer. By the coalescence of adjoining ulcers the greater part of the mucous membrane of the large and small intestine may become destroyed. The process is not confined to the mucosa and submucosa alone, but invades the muscular layers, and very frequently extends to the serous coat, which often presents numerous miliary tubercles over an area corresponding to the situation of the ulcer. From these there may sometimes be seen rows of tubercles extending along the lymphatics which lead from the diseased area to the mesenteric glands, which are usually caseous and considerably enlarged. The tuberculous ulcer then has the following characteristics: (*a*) It is irregular, rarely ovoid or in the long axis, more frequently girdling the bowel; (*b*) the edges and base are infiltrated, thickened, and often caseous; (*c*) the submucosa and muscularis are usually involved; and (*d*) on the serosa may be seen colonies of young tubercles or a well marked tuberculous lymphangitis. The mucous membrane surrounding the ulcers is generally the seat of more or less intense catarrhal inflammation, leading to a club-shaped or polyp-like hypertrophy of the villi of the small intestine and giving the mucous surface of the affected area a velvety appearance. Perforation and peritonitis are not infrequent events in the secondary ulceration. As a result of cicatrization of the ulcers stenosis of the bowel may occur, and in some instances a series of constrictions may be found.

Localized chronic tuberculosis of the ileo-cæcal region is of great importance. The cæcum frequently presents extensive ulceration of the mucous membrane, which not uncommonly extends into the appendix. As a consequence of the changes produced a definite tumor-like mass develops in the right iliac fossa. The tumor varies in size, is usually elongated in a vertical direction, hard, slightly movable, or bound down by adhesions and very sensitive to pressure. The disease simulates more or less closely a true neoplasm of this region, particularly carcinoma. The condition is characterized by gradual constriction of the lumen of the bowel, periodic attacks of severe pain, and alternating diarrhœa and constipation. In a few cases extirpation of the cæcum has been performed with fairly successful results. In a second form of this disease, occurring less frequently than the former, there is no definite tumor mass to be felt, but a general induration and thickening in the right iliac fossa similar to the local changes produced by a recurring appendicitis. In this variety a fistula discharging fecal matter occasionally results. Both forms may be distinguished from the diseases they simulate by the finding of tubercle bacilli in the stools or in the discharge from the fistula when such exists.

Tuberculosis of the rectum possesses special interest in connection with fistula in ano. According to Spillman's statistics, this complication occurs in about 3.5 per cent. of cases of pulmonary tuberculosis. Hartmann comparatively recently reviewed this subject and found the percentage even higher. In 626 patients suffering from pulmonary tuberculosis fistula in ano was present in 33 cases or in 4.91 per cent. He also found that the condition varied with sex, being more frequent in males. In 447 males it was present in 27 instances, or 6 per cent., whilst it occurred in only 6 cases out of 179 females, or 3.35 per cent. He also believes that the disease is due to a surface infection by fæces containing tubercle bacilli, and states that tuberculous diarrhœa appears to play an important part as an etiological factor. Fistula in ano was present 8 times in 114 individuals who had diarrhœa. The lesion has in many instances been shown to be tuberculous. It is very rarely primary, but if the tissue on removal contains bacilli and is infective, the lungs are almost invariably found to be involved. There is a general opinion that pulmonary symptoms may develop rapidly after the fistula is cut, but Hartmann thinks this view is exaggerated. There may be some foundation for the statement if the operation consists only in laying open the tract without freely excising the diseased area. Many of the cases of ischio-rectal abscesses are tuberculous and secondary in origin to a tuberculous rectal ulcer. More or less extensive ulceration of the rectal mucous membrane is often met with, and one has to bear in mind the possibility of cicatricial contraction arising therefrom.

(3) *Secondary tuberculous ulceration of the intestines* may be excited by extension of the disease from the peritoneum. The affection may be primary in the peritoneum or extend from tuberculous Fallopian tubes in women or from the mesenteric glands in children. Owing to the tuberculous process in the peritoneum the intestines become matted together, caseous and suppurating foci develop between the folds, and perforation into the lumen of the intestine may take place between the coils.

TUBERCULOSIS OF THE LIVER.

This affection of the liver is manifested in several different forms. Orth believes that the parenchyma of the liver cannot be a favoring soil for the development of the bacilli, as one rarely sees in this organ such extensive destructive changes as are met with elsewhere in the body. The organ is very constantly involved in—

(*a*) General tuberculosis. The miliary granulations are very small, and in acute cases scarcely to be recognized with the naked eye. Occasionally a few small tuberculous foci are found in the liver in chronic pulmonary tuberculosis. In such cases the tubercles are distributed throughout the substance of the organ, suggesting strongly that infection has occurred by the way of the blood. The liver is pale and very often fatty.

(*b*) A very interesting condition of the organ is produced by the development of tubercles in the finer bile vessels. According to Orth, such a condition may be found in association with general tuberculosis of the liver or it may occur independently. The tubercles may attain a considerable size, at times as large as hazelnuts. The centres soften and cavities are formed which are usually filled with a yellowish brown or greenish bile-stained caseous material. The organ may be honeycombed with these tubercular abscesses. Considerable difference of opinion appears to exist as to whether infection in this form is through the blood or by way of the excretory ducts. Simmonds is inclined to think that tubercles develop in the outer part of the bile ducts, and then open later into them. Pillet thinks that biliary tuberculosis in all its forms, from the small granulation to the true cavity, is an ulcerative process, the infective agent being carried by the excretory channels. He states that it differs anatomically from the most common form of tuberculosis of the liver, in which the infection is carried by the blood current, and that a complete analogy exists between this form of tuberculosis and that found in the lung.

(*c*) Occasionally, large coarse caseous masses are found in the liver in association with perihepatitis or tuberculous peritonitis. They may attain the size of an orange or larger.

(*d*) With the eruption of miliary tubercles there may be slight increase in the connective tissue, producing a tuberculous cirrhosis, which is often obscured by the fatty change. In all the chronic forms of tubercle in the liver there may be an overgrowth of fibrous tissue. Hanot has described several varieties, and believes that the condition may be primary. Practically, it is an extremely rare condition, except in connection with chronic tuberculous peritonitis and perihepatitis, when the organ may be much deformed by sclerosis involving the portal canals. A few cases of nodular diffuse hepatitis have been recorded in which the condition was associated with caseous pulmonary tuberculosis, without there being any evidences of localized tuberculous lesions in the liver itself. In such instances it has been suggested that the tuberculous toxin circulating in the blood acts as an irritant on the liver, thus producing an increase in the connective tissue. In this group symptoms of ascites may appear.

(*e*) It is now believed by some that localized areas of necrosis of the liver substance occur in tuberculosis similar to those found in this organ in typhoid fever and diphtheria. Hanot (in 1893) called attention to a peculiar lesion observed by him in the liver of several tuberculous patients in the form of small yellowish knots. They did not present the structure of tubercles, and no giant cells were to be found in them. In these areas, however, he was able to demonstrate tubercle bacilli, and he thinks that they constitute a peculiar form of hepatic tuberculosis.

TUBERCULOSIS OF THE PANCREAS.

According to Bécourt, the first account of tuberculosis of the pancreas was given in 1812 by Harles, who described the affection under the name of "pancreatic phthisis." The disease is very rare, always secondary, and generally associated with tuberculosis of the lungs, intestines, or mesenteric glands. A number of cases have been described as tuberculosis of the pancreas that were really due to tuberculous involvement of the lymph glands, either partially or wholly imbedded in the interstitial connective tissue of the pancreas. Lombard found tuberculosis of the pancreas 5 times in 100 autopsies on infants who died of tuberculosis. Klebs has claimed that disseminated miliary tubercles of the gland do not occur in general miliary tuberculosis. Orth, however, admits the occurrence, but says that it is exceptional. More frequently, he says, a partial miliary tuberculosis is seen in the vicinity of large caseous foci in the pancreas. In the pancreas of a child twenty-three months old, dead of general miliary tuberculosis, Barlow found tubercles whitish in color, the size of a pin's head, which showed commencing caseation in the centre.

Apart from the eruption of miliary tubercles, pancreatic tuberculosis presents itself in two forms: First, the infiltrated gland presents multiple foci. Infection in this variety takes place by the general circulation. The gland is enlarged and presents nodular masses which are often caseous. The gland substance between the foci may be healthy or it may show the presence of miliary tubercles for some distance about the diseased area. In the second variety the gland presents definite tuberculous abscess cavities, as in Aran's 2 cases, where the abscesses were about the size of a hen's egg. In these cases infection is supposed to occur by way of the pancreatic duct from the intestine.

There is no definite symptomatology, as the disease is invariably associated with tuberculosis of other organs. Aran states that salivation and eructation of fluid resembling saliva are symptoms which are very suggestive of pancreatic tuberculosis. Pemberton claims that emaciation is more marked in this affection than in any other disease. Bouillaud records a case where there was an enormous dilatation of the gall bladder, produced by compression on the common duct by a tubercular mass situated in the head of the pancreas.

VI. TUBERCULOSIS OF THE GENITO-URINARY SYSTEM.

Any organ of the genito-urinary system may be invaded; in comparatively rare instances one part only is found tuberculous, while in the majority of cases the process involves two or more parts of the tract. The successive involvement of the organs may be so rapid that unless the case has been seen early it may be impossible to state with any degree of certainty which has been the primary seat of infection. Especially is this the case when the disease is secondary to a tuberculous focus elsewhere in the body. There may be simultaneous involvement of various portions of the tract. While clinical and pathological experience has taught us that tuberculosis of the genito-urinary system may be primary, one always has to bear in mind the possibility of latent disease elsewhere in the body. Thus, as Bollinger says, tubercle bacilli may gain admission at some part of the respiratory tract without producing any lesion at the point of entrance, and finally reach a bronchial gland, where they set up a tuberculous process of extremely slow development without producing any symptoms. From this point bacilli may enter the blood stream and lodge in the epididymis or testicle proper, and produce nodules which are readily discovered, owing to the ease with which these parts are examined. Such a case might be quite easily mistaken for one of primary genital tuberculosis, whereas the true primary tuberculous focus is far distant. Thus it is practically impossible, without the information afforded by an autopsy, to state positively whether or not one is dealing with a true primary uro-genital tuberculosis.

Infection of the genito-urinary tract occurs in various ways:

1. *By Hereditary Transmission.*—It has been met with in the fœtus. The comparative frequency of tuberculosis of the testicle in very young children suggests very strongly that the uro-genital organs may be involved as a result of direct transmission of the disease from the parents. If one accepts Baumgarten's views of hereditary transmission of tuberculosis, this method of infection would seem quite probable.

2. *By infection from areas of tuberculosis already existing in the patient.*

(*a*) *Infection through the Blood.*—Owing to the fact that many cases of uro-genital tuberculosis are found at autopsy associated with disease of some distant organ, particularly the lungs, it would appear most probable that in these cases infection has been through the bloodvessels. Jani's observations, which were published by Weigert after the author's death, strongly support this theory. In studying sections of the genital organs of patients who died of pulmonary tuberculosis he found tubercle bacilli in 5 out of 8 cases in the testicle, and in 4 out of 6 cases in the prostate, without, in any instance, finding microscopical evidences of tubercles in these organs. The bacilli lay, in the testis, partly within and partly close beside the cellular and granular contents of the seminal tubules, whilst in the prostate they were always situated in the neighborhood of the glandular epithelium.

(*b*) *Infection from the Peritoneum.*—This source of infection, in both men and women, is much more frequent than is commonly supposed. The intimate relationship between the peritoneum and bladder in both subjects and with the vesiculæ seminales and vasa deferentia in the male allows of a ready means of invasion of these organs by direct extension of the disease. The peritoneum is a frequent source of genital tuberculosis in the female. No doubt, many cases of tuberculosis of the Fallopian tubes originate from this source. The fact that the fimbriated extremity of the tubes is often most seriously involved points rather strongly in this direction, although this might be taken as a point in favor of blood infection, owing to its greater vascularity. Various observations go to show that the action of the cilia lining the lumina of the Fallopian tubes tends to attract particles introduced into the peritoneal cavity. Jani's observation is very interesting in this connection, as showing the possibility of tubercle bacilli entering the tubes from the peritoneal cavity without there being any tuberculous peritonitis. He found typical tubercle bacilli in the lumen, in sections of a normal Fallopian tube, in a woman who died of pulmonary and intestinal tuberculosis. The explanation advanced was that the bacilli made their way through the thin peritoneal coat from one of the intestinal ulcers, thus reaching the peritoneal cavity, and thence attracted into the Fallopian tube by the current produced by the of the cilia lining the lumen. The intimate relationship between culous peritonitis and tuberculosis of the Fallopian tubes the fact that the latter are affected in from 30 to 40 per cent. of the cases.

(c) *Infection from Other Organs by Direct Extension.*—The occurrence of direct extension from the peritoneum has already been mentioned. In tuberculous ulceration of the intestine or rectum adhesions to the bladder in the male or to the uterus and vagina in the female may occur, with fistulæ and a direct extension of the disease resulting. Perirectal tuberculous abscesses may lead to secondary involvement of some portion of the genito-urinary tract. It must not be forgotten that tuberculosis of the vertebræ may be followed by tuberculosis of the kidney as a result of direct extension of the disease.

3. *By Infection from Without.*—Whether uro-genital tuberculosis may occur as a result of the entrance of tubercle bacilli into the urethra or vagina is still a disputed question. That bacilli gain admission to these passages during coitus with a person the subject of uro-genital tuberculosis, or by the use of foul instruments or syringes, seems quite probable. The possibility of genital tuberculosis occurring in the female as a result of coitus with a male the subject of tuberculosis in some portion of the genito-urinary system was first suggested by Cohnheim, who stated, however, that it rarely if ever occurred. Gärtner obtained important results from his experiments in animals. He found in experimenting with rabbits and guinea-pigs that a certain percentage of the females developed genital tuberculosis as a result of consorting with male animals with artificially produced tuberculosis of the testes and whose semen contained tubercle bacilli. The experiments of Oncarani and of Williams are directly opposed, however, to those of Cornil and of Dobrolansky, who claimed to have produced tuberculous endometritis by the injection of pure cultures of tubercle bacilli into the vagina of rabbits.

In a patient with intestinal tuberculosis the tubercle bacilli might accidentally reach the urethra or vagina from the rectum.

Uro-genital tuberculosis is commonest between the ages of twenty and forty years—that is, during the period of greatest sexual activity. Males are affected much more frequently than females, the proportion being 3 to 1. This great difference is no doubt partly due to the more intimate relationship between the urinary and genital systems in the former than in the latter. In the male the urethra forms the common outlet for the two systems, whilst in the female there is a separate outlet for each.

Once the uro-genital tract has been invaded, the disease is likely to spread rapidly, and the method of extension is an important one. Quite frequently there is direct extension, as when the bladder is involved secondarily to the kidney by passage of the disease along the ureter, or where the tuberculous process extends along the vas deferens to the vesiculæ seminales. No doubt surface inoculation occurs in some instances, and to this cause may be attributed a certain percentage of cases of vesical and prostatic disease following tuberculosis of the kidney. Although this probability is acknowledged, there is an element of doubt as to the possibility of the kidney becoming affected secondarily to the bladder or prostate by the direct passage of the bacilli up the lumen of one ureter; for in such a case we have to suppose that a non-motile bacillus, contrary to the laws of gravity, ascends against an almost constant current of urine flowing in the opposite direction. The lymphatics may afford a means for the spreading of the disease, but in a greater number of cases than is generally supposed the disease spreads by way of the bloodvessels. Cystoscopic examinations of the bladder not infrequently show the presence of tubercles beneath the mucous membrane before there is any evidence of superficial ulceration—a fact suggesting strongly a blood infection.

The discovery of tubercle bacilli in the urine and the obtaining of tuberculous lesions in animals as a result of inoculation with the urinary sediment afford us the only positive evidence of genito-urinary tuberculosis. So far, there are no authentic accounts of tubercle bacilli having been found in the semen of men with tuberculosis of the testicle or vesiculæ seminales. Owing to the fact that the smegma bacillus has the same staining reaction as the tubercle bacillus, and, morphologically, is practically indistinguishable from it, the greatest care must be used in obtaining the specimen of urine for examination, to eliminate, if possible, all chances of contamination. Thus the urine examined must be a catheterized specimen, and even then one runs the risk of carrying back into the bladder on the end of the catheter a few bacilli which may be washed out in the stream of urine and be mistaken for tubercle bacilli in the sediment. Repeated examinations should be made if the first specimens are negative, for, as Koch and Baumgarten have shown, the bacilli are not situated on the surface of an ulcer, but just beneath the portion which is undergoing coagulation necrosis, so that the chances are not great for the bacilli to be washed off in large numbers by the current of urine. Grethe[1] recommends a method for differentiating between tubercle and smegma bacilli, which depends upon the fact that the latter decolorize in alcohol much more readily than the former. The cover-slip preparations are stained in the usual way with carbol fuchsin. They are then treated for two minutes in a 20 per cent. solution of nitric acid, and afterward washed for ten minutes in alcohol (the strength of which is not mentioned). Any red stained bacilli left in the preparation must be tubercle bacilli, because smegma bacilli are completely decolorized by the use of the alcohol for a period of only five minutes. For practical use, Grethe recommends very highly Weichselbaum's method of staining tubercle bacilli. The preparation is first stained in carbol fuchsin, and then counterstained in a concentrated alcoholic solution of methylene blue. By this method, with the exception of the tubercle bacilli, the whole preparation, including the smegma bacilli, is stained blue, the tubercle bacilli appearing as red rods on a blue background. Inoculations of guinea-pigs with the urinary sediment will occasionally produce typical tubercular lesions when repeated examinations of the sediment for bacilli have given negative results.

TUBERCULOSIS OF THE KIDNEYS (PHTHISIS RENUM).

Not infrequently at autopsies on persons who have died of general tuberculosis the kidneys are found to contain miliary tubercles scattered throughout the substance of the organs. When death has occurred from pulmonary tuberculosis it is also quite common to find a few tubercles, or, in rarer instances, there may be a tuberculous pyelitis. In primary tuberculosis of the kidney, which is not very rare, tubercles usually first appear beneath the mucous membrane of the pelvis and in the papillæ. In secondary tuberculosis, occurring as a result of infection through the bloodvessels, the tubercles at first may be more or less generally scattered throughout the substance of the organ, or they may be localized either in the cortex near the capsule or beneath the mucous membrane of the pelvis. Where the kidney is involved as a result of direct extension of the disease along the ureter from some focus lower down in the urinary tract the mucous membrane of the pelvis and the adjacent kidney substance are first attacked. Occasionally renal tuberculosis follows tuberculous disease of the testicle, and infection may occur by the roundabout route of the lymph channels. The lymphatics of the testicle on their way to empty into the lumbar glands accompany the spermatic veins to their termination, and receive collateral branches from the ureters, and, not infrequently, trunklets which drain the perirenal fat and the capsule of the kidney. This permits of a direct route for the bacilli to reach the kidney from the testicle, in which instance the cortex would be first most seriously involved. In the majority of cases of renal tuberculosis the process also involves the pelvis and ureter, and sometimes the bladder and prostate. In advanced cases, in which the bladder, prostate, and vesiculæ seminales are also involved, it may be almost impossible to state whether the disease has crept from below upward along the ureters or whether it has started in the kidneys and proceeded downward. In the majority of instances I believe the latter is the case, and that infection takes place through the blood.

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[1] *Fortschritte der Medicin*, May 1, 1896.

Renal tuberculosis is most common during the middle period of life, although it may occur at the extremes of age. It is about twice as frequent in men as in women. One kidney alone may be involved, and the disease may creep down the ureter and extend a few millimetres on the vesical mucosa, as in a man with aortic insufficiency in whom, at autopsy, a localized patch of tuberculosis was found in the pelvis of the kidney, involving a pyramid, while the ureter five centimetres from the bladder and at its orifice was thickened and tuberculous. The prostate showed an area of caseation: there was no lung disease.

Taking as a type of the disease a case in which the tuberculous process begins in the vicinity of the pelvis of the kidney, the tubercles will first be found beneath the mucous membrane of the calyces and in the pyramids. The colonies of tubercles rapidly extend on the mucous membrane of the pelvis and spread throughout the substance of the pyramids. Necrosis and caseation proceed rapidly, and, as a rule, from the first it is a tuberculous pyo-nephrosis. The process extends from the medullary portion of the kidney to involve the cortex, and the whole kidney becomes converted into a series of cysts which correspond more or less accurately with the pyramids and the portions of the cortex corresponding to them. These cysts may, for a considerable time, remain separate, but eventually they communicate, owing to the thin portion of kidney substance between them being destroyed. The capsule of the kidney becomes greatly thickened. The cysts generally contain a cheesy substance resembling putty, which may eventually become impregnated with lime salts. In other instances the walls of the pelvis are thickened and cheesy, the pyramids eroded, and caseous nodules are scattered throughout the substance of the organ, even to the capsule, which may be thickened and adherent. In the rarer cases, in which the tuberculous process begins in the periphery of the kidney, the cortex may show quite advanced changes before the mucous membrane of the pelvis is involved to any extent. The disease may be confined to one kidney or progress more extensively in one than in the other. The less seriously affected kidney may only show a pyelitis or a superficial necrosis of one of the pyramids. On the other hand, one kidney, although not showing a tuberculous process, may be the seat of a serious nephritis, probably an advanced amyloid degeneration. The ureters are usually thickened and the mucous membrane ulcerated and caseous. Involvement of the bladder, vesiculæ seminales, and testes is not uncommon in males.

The symptoms of renal tuberculosis are variable, but they are practically those of pyelitis. The condition is for many years compatible with fair health. The urine may be purulent for a long period, and yet the patient may have little or no distress. With our present knowledge it is impossible to distinguish accurately cases in which the eruption of tubercles first occurs in the vicinity of the pelvis from those in which the cortex is first attacked. Fenwick, however, claims that in the pelvic form blood and pus appear in the urine in small amounts, either coincidentally with renal pain or soon after its appearance; that renal colic appears relatively earlier than in the cortical form; that the stages of the disease are passed through more rapidly; and that the bladder is earlier involved. When, however, the tuberculosis primarily attacks the cortex, it must first break into the pelvis before very characteristic symptoms are produced. Polyuria, resulting from the irritating effect of the minute tubercles, would probably be the first symptom complained of, even before any aching in the kidney is experienced. The urine would be of low specific gravity, and would contain more albumin than could be accounted for by the presence of the trace of pus. Hemorrhage from the two situations also varies. In the early stage of the pelvic form the bleeding is usually slight and intermittent, whereas when a cortical deposit sloughs out suddenly into the pelvis there may be profuse but transient hæmaturia. In renal tuberculosis, when the bladder becomes involved, or even earlier, micturition is frequent, and many cases are mistaken for cystitis. The possibility of nature affecting a cure is shown by the accidental discovery of the so-called scrofulous kidney, in which the organ has become converted into a series of cysts filled with a putty-like substance. When the disease becomes advanced and both organs are affected constitutional symptoms are more marked. There is irregular fever, with rigors and loss of weight and strength. Recurrent chills are common. General tuberculosis is frequent. In only one of my cases were the lungs uninvolved. Occasionally a cyst may perforate and cause general peritonitis. The pain suffered varies greatly: it may be of a dull, aching character, situated over the region of the affected kidney, or, as occasionally happens.

severe and colicky, owing to the plugging of the ureter by some of the caseous material.

Physical examination may detect special tenderness on one side, or the kidney may be palpable in front on deep pressure; but tuberculous pyelo-nephritis seldom causes a large tumor. Occasionally the pelvis becomes enormously distended, but this is rare in comparison with calculous pyelitis. The urine presents changes similar to those of ordinary calculous pyelitis—pus cells, blood, epithelium, and occasionally definite caseous masses, and even moulds of the pelvis. Albumin is present in considerable quantity, but tube casts are not commonly seen. Careful and persistent examination of the urinary sediment for tubercle bacilli will usually demonstrate their presence.

The very close resemblance between calculous pyelitis and renal tuberculosis, both in the gross pathological changes and in the symptoms produced, renders it in many instances extremely difficult to distinguish between the two affections. Hæmaturia occurs in both, but in tuberculous disease it occurs less frequently, is not so profuse, and is less influenced by exercise than is the hæmaturia of calculous pyelitis. Renal colic is not so frequent as in the latter affection. The presence of tuberculosis elsewhere in the body, particularly in a testis or the prostate, and the discovery of tubercle bacilli in the urine, should leave little doubt as to the true nature of the disease.

TUBERCULOSIS OF THE URETERS, BLADDER, AND URETHRA.

It is doubtful whether primary tuberculosis of a ureter ever occurs. It is almost invariably involved secondarily to some other part of the genito-urinary system, particularly the pelvis of the kidney. The disease usually occurs as a result of a direct extension of the tuberculous process from the kidney, or in rarer instances from the bladder by extension upward. Surface inoculation by bacilli contained in the urine from a tuberculous kidney no doubt often occurs. In advanced cases the whole of the mucous membrane of the ureter may be extensively ulcerated and the walls thickened and caseous. In such a case it is quite possible on deep palpation to feel the ureter as a thickened, more or less irregular cord.

Tuberculosis of the bladder is quite common. It may be primary, but is generally secondary to tuberculosis elsewhere in the uro-genital tract. Extension of the disease from the kidney may occur in various ways:

First, by surface inocculation. The urine coming from a tuberculous kidney is laden with irritating products, which finally cause swelling and congestion of the vesical mucous membrane, particularly over the trigone. This leads to frequency of micturition, owing to irritation of the vesical neck. Later excoriation of the surface occurs or an abrasion of the mucous membrane is produced by needless instrumentation. The soil having been thus favorably prepared and a means of entrance for the bacilli produced, infection readily takes place. In such cases, therefore, if the mucous membrane remains intact, the chances of infection are much diminished, so that every possible means of ascertaining the true cause of the bladder trouble should be adopted before sounding for stone is performed.

Secondly, the bladder may be involved as a result of direct extension of the disease along the line of the ureter. The mucous membrane about the orifice of the urethra becomes swollen and congested, and this is followed by ulceration, which gradually extends along the corresponding trigonal limb.

Thirdly, in a great many more instances than is generally supposed the bladder is involved secondarily to renal tuberculosis as a result of infection through the bloodvessels. Cystoscopic examination of the bladder in suspected cases quite frequently shows the presence of tubercles beneath the mucous membrane without there being any superficial ulceration—a point strongly suggesting a blood infection.

The disease sometimes extends from the prostate, the infection creeping rather uniformly up from the anterior angle of the trigonum. The spread of the disease probably takes place along the lymphatics of the submucous coat. Occasionally the bladder is invaded from an infected seminal vesicle. Not infrequently there is a direct extension of the disease from the recto-vesical fold of peritoneum in cases of tuberculous peritonitis. Tuberculous ulcerations of the intestine may lead to adhesions to the bladder with secondary involvement of the latter. In the female, invasion may be from a tuberculous uterus or vagina.

The extent to which the tuberculous process may have advanced varies considerably. In primary vesical tuberculosis the middle coat alone may be found involved if the disease has not become too far advanced. Other cases may show only a slight localized ulceration, or the whole of the vesical mucous membrane may present irregular, deep ulcerations, the bases of which are covered with a caseous exudate. The bladder is usually contracted and the walls very much thickened. The urine is purulent and contains particles of caseous material.

In primary tuberculosis of the bladder the symptoms produced may not appear until some considerable time after involvement. When they do present themselves, however, the resemblance to those caused by calculus may be quite marked, especially when the tuberculosis begins in the posterior wall. Frequency of micturition and pain in the glans or mid-penis, particularly in the latter situation, are usually the first symptoms which attract the patient's attention. Fenwick found these to be the earliest symptoms in 76 per cent. of his cases, whilst in many of the remainder hemorrhage was the first symptom. The frequency of micturition is at first most marked during the day, but later the night is also disturbed by repeated calls to empty the bladder—a point which would be strongly against the probability of the symptoms being due to a calculus. These symptoms are followed in from a few days to a few months, according to the acuteness of the disease, by the appearance of blood in the urine. This varies in amount, and may consist of a few drops at the end of micturition. The hemorrhages are usually transitory, and are not specially influenced by rest, as are those of vesical calculus. Pus is usually present in the urine from the beginning, at first in small amounts, but increasing in quantity as the disease advances. During the act of micturition the stream is often suddenly arrested, the patient checking it voluntarily, owing to the severe pain and spasm. This differs from the stoppage of the stream by a calculus engaged in the mouth of the urethra, which is beyond the patient's control and which usually increases the pain. The frequency of micturition, which was at first due to the vesical irritability and exaggerated "distention reflex," is later partially produced by the diminished capacity of the bladder, owing to the gradual contraction.

In advanced stages of vesical tuberculosis the symptoms are much the same whether the infection is primary or secondary. Protracted cystitis, which has come on without apparent cause, is always suggestive of tuberculosis. The renal regions, the testes, and the prostate should be examined with care. The judicious and careful use of the cystoscope is of infinite value in arriving at the true nature of the disease if repeated examinations of the urinary sediment have given negative results.

Tuberculosis of the urethra, as a primary infection, is extremely rare. Secondary tuberculosis, which is more common, may result from direct invasion from the prostate by continuity or by surface inoculation or by blood infection from a focus higher up. Miliary tubercles in the urethra are not uncommon in patients who die of general miliary tuberculosis. The chief symptoms of urethral tuberculosis are excessive pain on urination or instrumentation and a marked tendency to bleeding on slight manipulation. When definite ulceration occurs the first ounce or two of urine passed nearly always contains tuberculous detritus. Primary tuberculosis of the urethra may strongly simulate stricture, but the extraordinary amount of pain caused by the most delicate instrumentation, even after the use of a strong solution of cocaine, should lead one to suspect tuberculosis.

TUBERCULOSIS OF THE PROSTATE AND VESICULÆ SEMINALES.

The prostate is frequently involved in tuberculosis of the uro-genital tract, some writers claiming that it never escapes. In Krzyincki's cases it was affected in 14 out of 15 males. In 37 males Orth found the prostate involved in 17 cases.

The disease may occur as a primary infection, but more commonly results from extension from some adjacent or distant organ. Many cases of primary tuberculosis of the prostate follow chronic follicular inflammation of the gland. The lowered resistance produced by such an inflammation seems to be an important determining factor. In certain instances prostatic tuberculosis appears to date from an attack of gonorrhœa. The involvement of the posterior urethra in the gonorrhœal inflammation excites into activity any slumbering tubercular focus which may be already existent in the prostate. Secondary infection generally follows tuberculous involvement of the testes, bladder, or kidney. That following testicular disease is commonest of all. More marked changes occur in primary tuberculosis of the prostate and in cases in which the disease is secondary to involvement of adjacent parts than in those in which it is secondary to pulmonary tuberculosis, for in the latter case death is likely to occur before the prostatic disease becomes far advanced.

In primary tuberculosis of the organ the tubercles generally first appear about the acini of the glands, although occasionally the submucous tissue of the prostatic urethra may be invaded. In the latter instance the deposit undergoes caseation, and leads finally to a superficial ulceration of the mucous membrane, thus permitting of a mixed infection, owing to contamination with pus organisms, after which the destructive process is likely to advance more rapidly. In some instances the entire prostate may be converted into an abscess cavity which may open into the urethra, and this is followed sometimes by extravasation of urine. Secondary prostatic tuberculosis begins in the periprostatic lymphatics and bloodvessels. In both primary and secondary infections extension of the disease into the surrounding tissues frequently occurs, and quite often sinuses burrow in various directions. The commonest situation for these sinuses to open is on the perineum just in front of the anus, or they may burrow backward and open into the rectum. Occasionally one sees evidences of a spontaneous cure in the occurrence of calcareous and fibro-sclerotic changes in the cavity wall, with a resorption of their contents and a contraction of the entire mass.

Enlargement of the prostate is more or less marked from the commencement of the disease. In primary infections the enlargement is general, and in a majority of cases uniform. Where the infection is secondary to tuberculosis of the testicle on one side, the corresponding half of the prostate is usually considerably larger than the other. The enlargement is partly due to the growth of tubercles, and partly to secondary inflammation and hypertrophy of the interstitial connective tissue.

If the disease begins in the periphery of the prostate or in the periprostatic tissue, the symptoms may be for a long time delayed. Complaint is not likely to be made until the urethra or neck of the bladder is invaded. Frequent and painful micturition, increasing in severity as the vesical neck becomes involved, is the most uniform symptom. There may be hæmaturia, which is usually slight, however, excepting in rare instances. The urine contains some pus, which may be markedly increased for a time, when a prostatic abscess opens suddenly into the urethra. Agonizing pain is experienced on catheterization. A rectal examination gives valuable information, and, next to finding tubercle bacilli in the urinary sediment, affords the most positive evidence of the true nature of the disease. In the early stages only a few small tubercles may be felt, but in more advanced cases hard, irregular nodules, varying in size from a pea to a bean, and occasionally areas of softening, may be easily detected. If the vesiculæ seminales are also enlarged and nodular, the evidence will point still more strongly toward tuberculosis. The importance of a rectal examination in all cases of suspected genito-urinary tuberculosis cannot be overestimated, owing to the frequency with which the prostate is involved, no matter in what part of the tract the primary focus may be situated.

Involvement of the vesiculæ seminales is quite common in uro-genital tuberculosis. They were involved in 11 out of 15 males in Krzyincki's series of cases. Primary infection rarely if ever occurs. The disease is usually secondary to tuberculosis of the testicle or prostate, the former source of infection being the commonest. Direct extension from a tuberculous peritonitis occurs. The seminal vesicles become enlarged, hardened, and the nodular character can be quite readily made out on rectal examination. Not infrequently the tuberculous deposit breaks down with the formation of distinct cavities within the seminal vesicle—a condition occasionally seen at autopsy.

TUBERCULOSIS OF THE TESTES.

This is a somewhat common affection, and may be primary, or, more frequently, is secondary to tuberculosis elsewhere. It occurs quite frequently in young children, many cases occurring before the second year. It is also stated to have been found in the fœtus. In infants it is serious, and usually associated with tuberculosis in other parts. A general infection was present in every one of the 9 cases reported by Hutinal and Deschamps. In 20 cases reported by Jullien 6 were under one year, and 6 between one and two years of age. In 5 cases both testicles were affected. Koplik holds that a majority of the cases of this kind are congenital in Baumgarten's sense. Many cases also occur about puberty and in young adult life. In primary tuberculosis of the testicle and in cases in adults which are secondary to tuberculosis of adjacent parts, the epididymis is generally first involved, and the process usually begins in the globus major. Where the testicle is involved as a part of a general miliary tuberculosis the tubercles may appear simultaneously in the epididymis and testicle proper. In children the tunica albuginea is first affected, but in adults the disease commences in the substance of the organ, the gray miliary tubercles appearing in the lymphoid intertubular tissue of the epididymis, and often later working their way through the mediastinum testis and infecting the lymphoid tissue around the tubuli seminiferi.

The beginning of the disease is rarely noticed. A hard nodule, already of some size, is usually discovered accidentally at the back of the gland. When both testicles are involved the process in one is usually more advanced than in the other. As the disease progresses the nodules increase in size, and eventually some may undergo caseation and softening. Occasionally in this way the whole testicle may become destroyed. The skin at one point may become adherent, reddened, and inflamed, finally giving way and allowing the tuberculous abscess to discharge. Where such a condition occurs over the body of the gland a hernia testis may follow. Caseation, however, does not always occur, but in rare instances the gland undergoes calcification and fibroid degeneration with complete healing.

The disease not infrequently extends along the vas deferens, and finally involves the vesiculæ seminales, prostate, and bladder. When involvement of the vas occurs it will be found distinctly thickened and nodular.

Tuberculosis of the testicle is only slightly painful and there is very little tenderness on palpation. Excepting in very advanced stages of the disease testicular sensation is retained. Hydrocele very rarely occurs. The disease is most likely to be confounded with syphilis. In the latter, however, the body of the gland is often affected. There is no pain nor tenderness, but the testicular sensation is lost early. The outlines of the growth are more nodular and irregular. The vas is never affected in syphilitic disease of the testicle. It is not uncommon to have tuberculosis of the testicle associated with peritoneal tuberculosis, and in an obscure peritoneal affection the detection of nodules in the testicle has often led to a correct diagnosis. General infection may follow tuberculosis of the testicle, and also, in some instances, may result from removal of a diseased gland.

TUBERCULOSIS OF THE FEMALE GENERATIVE ORGANS.

The reproductive organs of the female have for a long time been known to be occasionally the seat of tuberculosis, but it is only within the last few years that tuberculous affections of these parts have been recognized as comparatively frequent occurrences. Laparotomy in tuberculous peritonitis has revealed the fact that in very many instances in women the Fallopian tubes are also involved. This discovery has excited interest in the subject, owing to the strong probability that the tubes may be in many instances the source of origin of the peritoneal disease.

The careful and systematic microscopic examination of specimens from the operating room and autopsy table has shown that primary tuberculosis of the tubes is not at all uncommon, and that many cases, which macroscopically would appear to be of a simple inflammatory character, are really tuberculous (J. Whitridge Williams).

Genital tuberculosis in the female, as has already been stated, is much less frequent than in the male, the proportion being 1 to 3. The disease is most common between the ages of twenty and forty years—that is, during the period of greatest sexual activity. Cases have occurred as early as ten weeks and as late as eighty-three years of age. Although statistics vary considerably, the frequency of genital tuberculosis may be judged from the fact that various pathologists have found it present in from 1 to 8.5 per cent. of all autopsies on phthisical women. Kelly had found tuberculosis present in 1 out of every 12 operations for the removal of tubes and ovaries which were the seat of past or present inflammatory disease. Certain portions of the genital tract are attacked much more frequently than others, the order of frequency being as follows: tubes, uterus, ovaries, vagina, cervix, and vulva.

Vulva.—Tuberculosis of the vulva is a rare occurrence, only 3 authenticated cases, in which tubercle bacilli were found or in which inoculation experiments gave positive results, having been reported up to 1893 (Williams). The vagina is practically always involved. The lesion produced exhibits all the characters of an ordinary tubercular ulcer. The presence of tubercle bacilli in the secretions or of tubercles in the scrapings from the ulcer would differentiate the disease from carcinoma or syphilis, for which it might be mistaken.

Vagina.—The vagina is usually involved secondarily to a tuberculosis of some portion of the genital tract higher up, particularly the uterus. It may, however, be the only seat of tuberculosis in the genitalia, and Friedländer claims that it may be the primary focus of the disease in the body. Occasionally it becomes involved secondarily to disease of the bladder or rectum by direct extension, in which case vesico-vaginal or recto-vaginal fistulæ not infrequently result. The upper third of the posterior wall of the vagina is usually involved, as this is the area with which the exudate from tuberculous foci higher up usually comes in contact. The disease may occur either as an eruption of miliary tubercles or as an ulcerating surface. Tuberculosis of the vagina might be mistaken for granular vaginitis, hard or soft chancre, carcinoma, or papular and ulcerative syphilides. Here, again, the microscope is of invaluable service in clearing up the diagnosis.

Uterus.—Tuberculosis of the body of the uterus is very rare and is nearly always secondary. It is generally associated with tuberculosis of the tubes, from which the process extends. The uterus, however, may be the only seat of tuberculous disease in the body. Rarely does the process extend beyond the internal os to involve the cervix. It may occur as a miliary tuberculosis, with or without the formation of ulcerations. In nearly all cases there is at first an eruption of miliary tubercles in the endometrium, a form of the disease met with particularly at autopsies on women who have died of some other disease, the condition never having been suspected during life. A few minute ulcerations may be present. The endometrium between the tubercles may be reddened or may appear normal. The form of uterine tuberculosis generally met with, however, is the chronic diffuse tuberculosis (caseous endometritis). Here the entire uterine cavity is filled with caseous material; the surface of the endometrium is covered with exudate, and presents irregular and jagged ulcers, the floors of which are studded with tubercles in various stages of development. Later the muscular wall of the uterus becomes infiltrated with tubercles and undergoes hypertrophy. The cervical canal may become obstructed by caseous exudate, and the latter, accumulating in the uterine cavity, produce a pyometra.

The *cervix* of the uterus is much less frequently involved than the body. It is seldom associated with disease of the latter, but not commonly occurs along with vaginal tuberculosis. Friedländer reported a case in which it was the only seat of tuberculosis in the body. The disease generally presents itself in the form of an eruption of miliary tubercles or as an ulcerating surface. In advanced cases the condition might be mistaken for carcinoma of the cervix, but the examination of sections of a minute portion of the diseased area would reveal the true nature of the disease.

Fallopian Tubes.—The Fallopian tubes are by far the most frequent seat of genital tuberculosis. In a large percentage of cases the disease is associated with tuberculosis of the uterus or ovaries or both. The special attention which has been paid to local affections of these parts by gynecologists during the last decade has taught us that primary tuberculosis of the tubes is not at all uncommon. The disease may produce a most characteristic form of salpingitis, in which the tubes are enlarged, the walls thickened and infiltrated, and the contents cheesy. The fimbriated extremity is usually closed, and the fimbriæ are frequently bound down to the ovary. When both ends of the tube become occluded a very large pus sac may result. Between this and the mildest cases, in which only a few visible tubercles are studded over the mucosa, all grades exist. The condition is usually bilateral. It may occur in quite young children.

Although, as a rule, the disease is evident on macroscopic examination, yet there are specimens which to the naked eye appear to be ordinary cases of salpingitis, but which on microscopic examination show the mucosa to be studded with numerous miliary tubercles (Welch and Williams). These cases of "unsuspected tuberculosis" constitute 75 per cent. of all the cases of tuberculosis of the Fallopian tubes which have been operated on in the gynecological department of the Johns Hopkins Hospital.

Tuberculous salpingitis may cause serious local disease with abscess formation, and it may be the starting point of peritonitis.

It is practically impossible to make an absolute diagnosis of tuberculosis of the tubes. The association of a thickened tube with an ill defined mass in the abdominal cavity should arouse one's suspicions.

Ovary.—Although comparatively rare, tuberculosis of the ovary is more common than was formerly supposed. It may be the only seat of tuberculosis in the genital tract, as is sometimes the case when found associated with tuberculous peritonitis. Primary tuberculosis of the ovary probably never occurs. The disease may manifest itself as an eruption of tubercles over the surface of the ovary, or there may be more extensive involvement with the production of an ovarian abscess.

VII. TUBERCULOSIS OF THE BRAIN AND CORD.

In connection with acute miliary tuberculosis a few scattered granules may be met with on the meninges. One of the special forms of acute tuberculosis affects the meninges, and has already been described. (See Acute Tuberculous Meningitis, page 754.)

The disease occurs in two forms in the brain—namely, a localized chronic meningo-encephalitis, in which there is thickening of the membranes and small nodular tubercles; and the larger tuberculous tumor, which may attain the size of a walnut or larger, and which is often solitary. These forms develop slowly, are essentially chronic, and have the clinical characters of a tumor.

The tuberculous brain tumor is met with most commonly in children. Of 148 cases collected by Bribram, 118 were under fifteen years of age. Tubercles are usually found in other organs as well, particularly the lungs and the bronchial glands. In a few rare cases the brain alone is involved. They are frequently multiple—in 100 out of 183 cases, according to Gowers; in 20 per cent., according to Starr. The growths range in size from a pea to a walnut; occasionally larger, somewhat diffuse masses are found. They are almost always attached to the meninges; rarely are deep in the brain substance. The masses may really look imbedded in the white matter of the cerebrum, but on section are found to be attached to the pia mater at the bottom of a sulcus. They occur most frequently in the cerebellum, next in the cerebrum, and then in the pons. The tuberculous tumor is, as mentioned, usually attached to the meninges, is grayish yellow in color, firm, hard on section, cheesy, yellow, and is often surrounded by a translucent connective tissue. The centre of the growth may be semi-diffluent. In other cases lime salts are deposited. The tuberculous growth may produce symptoms by causing destruction of, or pressure upon, the contiguous brain sub-

nce, or, growing about the arteries of the meninges, may block the
od current and cause areas of softening. Growing about the longi-
inal fissure, it may compress the sinus and lead to thrombus forma-
n ; and, lastly, it not infrequently excites a tuberculous meningitis.

The symptoms of tuberculous growths in the brain are those of
or. The occurrence in children, the coexistence of tuberculous
ions elsewhere, or the presence of a healed gland or joint disease
among the features which would suggest the tuberculous character
the growth.

Tuberculosis of the spinal cord occurs in the same forms as in the
in. Acute tuberculous meningitis is very rarely confined to the
d ; it is almost always cerebro-spinal. A tuberculous tumor in the
d is rare. Of 130 tumors of the cord collected by Lloyd, 15 were
bercle. Herter has reported 3 cases, and collected 24 instances from
e literature, in all of which save 1 the condition was secondary.

VIII. TUBERCULOSIS OF THE MAMMARY GLAND.

Excellent descriptions of tuberculosis of the breast were given by Astley Cooper in 1829, by Nélaton in 1839, and by Velpeau in 1854. For nearly three decades following the latter date very few cases were recorded, and it was not until the appearance of Dubar's monograph in 1881 that mammary tuberculosis became generally recognized. With the exception of histological details, Velpeau's account has never been surpassed. Tuberculosis of the breast is much more common than has hitherto been generally supposed. Mandy[1] has collected 40 cases, only 1 of which occurred in the male. Other cases of mammary tuberculosis in the male have been reported by Horteloup and Poirier. The disease is commonest between the fortieth and sixtieth years. It is said never to occur in children, but Payne observed a case in an infant which was also the subject of general tuberculosis. Traumata and conditions associated with the puerperal state seem to favor its development. The majority of cases occur in women who have borne children. Of 35 cases collected by Powers,[2] 22 were in married women, and of these 21 had borne children. The right breast appears to be oftener affected than the left. In only 1 of Powers' cases were both glands diseased.

Velpeau recognized that the disease may be either primary or secondary, and subsequent investigations have borne out his views. In primary cases it seems likely that infection takes place through the milk ducts, although the bacilli may enter from infected fissures by way of the lymphatics. The great majority of cases are secondary to some other focus in the body, usually the lungs.

Mammary tuberculosis occasionally occurs in the form of scattered nodules throughout the gland, resembling often, in the early stages, alveolar hypertrophy. Both the parenchyma and the stroma of the gland are involved, and the nodules may undergo caseation. A second variety of the disease occurs in the form of rather large caseous tumors, which on section closely resemble tuberculous lymph glands. These soften and break down, and frequently involve the skin. Fistulæ

[1] *Bruns' Beiträge*, viii.

[2] *Annals of Surgery*, 1894.

which discharge a thin caseous matter frequently develop. These, together with the ulcers, present a characteristic tuberculous aspect. The nipple is quite often retracted in the above forms. Mammary tuberculosis not infrequently takes the form of a cold abscess. The axillary glands are involved in about two thirds of the cases. The dangers to which children are exposed by sucking women who are the subject of tuberculosis of the breast is shown in a case reported by Nièpce,[1] in which a nurse whose milk contained tubercle bacilli suckled a child born of healthy parents, with the result that the child soon afterward died of tuberculous meningitis.

The disease runs a chronic course, lasting months or years. The diagnosis can be made by the general appearance of the fistulæ and ulcers and by the finding of tubercle bacilli. Simple opening of the abscesses, with scraping of the cells, is not sufficient. With a radical operation, in which the breast and axillary glands are thoroughly removed, the chances against secondary local recurrence are good.

The skin of the breast is occasionally the seat of lupus, which may affect either the areolar region or the skin elsewhere.

In 1836, Bedor described an interesting condition of the breast in subjects who suffered from pulmonary tuberculosis, in which the gland became temporarily enlarged, without there being any local tuberculous lesions. The condition has been quite frequently observed since that date. The enlargement is only temporary, disappearing in a few weeks. It is commonest in men, and usually only one gland is affected. The condition is usually found on the same side as the most advanced pulmonary changes. The breast is firm to the touch, and is often quite sensitive to pressure. Thomas[2] has collected several cases, and reports 1 himself in which the histological examination showed the enlargement to be due to the development of fibrous tissue about the acini, which were considerably atrophied.

IX. TUBERCULOSIS OF THE ARTERIES.

In chronic tuberculous disease of the lungs and other organs the arteries are often involved in an acute infiltration; tubercles may develop in the walls and proceed to caseation and softening, which may be followed by the formation of a thrombus, or hemorrhage may occur. The recent observations of Hektoen, referred to under Tuberculous Meningitis (page 756), show that there may be the production of tubercles of the intima, and a diffuse subendothelial proliferation due to the implantation of bacilli direct from the blood. By direct extension into vessels the bacilli are widely distributed. Tuberculosis of the smaller arteries plays a very important rôle in meningitis, in which from the adventitia the tuberculous disease may invade the media and intima and lead to occlusion or thrombus formation.

Primary tuberculosis of the larger bloodvessels is almost unknown. Occasionally the aorta is invaded from a cheesy mass in a lymph gland outside the vessel. In a case reported by Flexner a patient with chronic tuberculosis presented a nodular mass in the aorta 2.5 cm.

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[1] *Paris Thesis*, 1886.

[2] *Ibid.*, 1893.

below the origin of the left subclavian artery. It was pale, translucent, apparently made up of several smaller masses. It was found to be a tubercle seated directly upon the intima, and consisted of several masses with caseous centres. The most interesting feature was that both media and adventitia were perfectly normal. There were no caseous glands in the vicinity of the aorta.

Prognosis in Tuberculosis.

At one time or another tubercle bacilli effect a lodgement in a considerable proportion of all individuals, justifying the old German axiom: "*Jedermann hat am Ende ein bischen Tuberculose.*" Infection with the bacilli does not necessarily mean the establishment of a progressive and fatal disease. The subject is a wide one, and there are several aspects in which it may be considered:

(*a*) *The Natural or Spontaneous Cure of Tuberculosis.*—The spontaneous healing of local tuberculosis is an every-day affair. Disease of the bones, of the joints, and adenitis may heal without the aid of the knife or of medicines. The percentage of persons with evidence of tuberculous lesions, active or obsolete, is remarkably high. It is stated that in the autopsies at the Paris Morgue, made, as a rule, upon the bodies of persons who have committed suicide or who have been killed accidentally, nearly 75 per cent. show tuberculous foci—either calcareous or cheesy nodules in the mesenteric or bronchial glands, or puckering with caseous or calcareous nodules at the apices. The percentage in observations which have been made of late years on this point in hospitals has been very striking, as showing the widespread prevalence of the disease. In 1000 autopsies at the Montreal General Hospital, excluding the 216 cases dead of pulmonary tuberculosis, there were 59 cases which presented tuberculous lesions in the lungs. This estimate is low, as I excluded (which I really should not have done) the solitary cheesy nodule unless there were colonies of tubercles in the vicinity. These 59 cases died of various diseases and at various ages, a majority of them between forty and sixty years. My experience tallies closely with the larger figures of Heitler, taken from the Vienna post-mortem records, in which, of 16,562 cases in which the death was not directly due to pulmonary tuberculosis, there were 780 instances of obsolete tubercle. The more recent observations have shown a much higher percentage: thus, Bollinger found traces at autopsy of former tuberculosis in 27 per cent.; Massini in 39 per cent.; and Harris in 38.8 per cent. The spontaneous arrest of pulmonary tuberculosis is, after all, a very common affair. Clinically it is shown by the complete recovery of patients in whose sputa elastic tissue and bacilli have been found, and anatomically by the presence of lesions in all stages of repair. A clear distinction should be drawn between arrest and healing. The latter term may be applied when in the granulation products and associated pneumonia a scar tissue develops and the caseous areas become cretaceous. When the fibroid change encapsulates, but involves the entire tuberculous area, the tubercle may be called involuted or quiescent, but it is not harmless, as may be shown by the fact that usually about such apparently quiescent areas there are small colonies of miliary tubercles. Cavities of any size rarely heal, in the proper sense of the term. They may become greatly reduced in size, and an upper lobe of a lung with numerous cavities may be so contracted by sclerosis and shrinkage that it has not one third of its natural dimensions. Laennec described with great accuracy the natural process of cure in tuberculosis, and suggested that as tubercles in the glands heal, the same could take place in the lesions of the lungs. At the apices of the lungs the following common conditions are held to signify healed and obsolete tuberculous processes: (1) The thickening of the pleura, usually at the posterior surface of the apex, with subjacent induration for a distance of a few millimetres. This has, perhaps, no greater significance than the milky patch on the pericardium. (2) Puckered cicatrices at the apex—*cicatrices complètes* of Laennec—depressing the pleura and on section showing a large pigmented fibrous scar. The bronchioles in the neighborhood may be dilated, but there are neither tubercles nor cheesy masses. This may sometimes, but not always, indicate a healed tuberculous lesion. (3) Puckered cicatrices with cheesy or cretaceous nodules, and with scattered tubercles in the vicinity. (4) The *cicatrices fistuleuses* of Laennec, in which the fibroid puckering has reduced the size of one or more cavities which communicate directly with the bronchi.

(*b*) *The Factors of Prognosis in Established Pulmonary Tuberculosis.*—Many years ago Flint called attention to the self-limitation and intrinsic tendency to recover in well marked pulmonary tuberculosis. Of 670 cases, 44 recovered, and in 31 the disease was arrested. The factors upon which one may lay stress in estimating the prognosis in a case with well marked symptoms, say at one apex, are as follows: Previous good health and a sound family history are perhaps the most important. A strong digestion is a third most important favoring factor. A fourth, and perhaps most essential of all, is the possibility of living in a favorable environment. A slow, gradual onset without high fever and without rapid consolidation and caseation is also a good omen. Cases beginning with pleurisy appear to run a more protracted and favorable course. Of the special symptoms fever is perhaps the most valuable element. With apyrexia the local disease rarely makes much progress. The higher, the more irregular, and the more persistent the fever, cæteris paribus, the more grave is the prognosis. The facility with which the fever is reduced by the open-air treatment is another important point, as are also the frequency and severity of the recurrences of the pyrexia which are so common in the chronic forms of the disease. Recurring attacks of hæmoptysis are unfavorable, more particularly when they are followed by spells of high fever. Not very much stress is to be laid upon the number of bacilli in the sputa, since they may be extraordinarily abundant from a very small focus of local disease. On the other hand, persistence for a long period in very large numbers is usually an unfavorable element in prognosis, while a gradual diminution is a hopeful feature. In pulmonary tuberculosis the *primæ viæ* control the situation, and the better the digestion and the more able the patient is to take a varied and nourishing diet the better are his prospects. There are no more unfavorable cases than those in which, early in the disease, with pronounced gastric symptoms, there is a marked chloro-anæmia.

(*c*) *The Duration of Pulmonary Tuberculosis.*—Laennec placed the erage duration at two years. As mentioned, a case of acute pneu-nic phthisis may prove fatal within ten days, whereas in the chronic m the disease may persist for twenty or more years. The probable ation in each individual case must be estimated according to the actors already mentioned. The large statistics of different authors vary very much; thus in Pollock's tabulation of over 3500 cases the ean duration of the disease was a little over two years and a half. Williams's returns for 1000 patients in the better classes give only 198 deaths, and the mean duration of life in the latter after the com-encement of the disease was seven years and eight months, while only 6 per cent. of these patients lived less than nine years. Of the survivors, the average duration of whose life was eight years and two months, as many as 68 patients, or 8 per cent. of the whole number, had lived more than twenty years from the commencement of the disease" (Wilson Fox).

(*d*) *Tuberculosis and Marriage.*—Under the subject of prognosis comes the question of the marriage of persons who have had tuberculosis or in whose family the disease prevails. The following brief statements may be made with reference to it:

(1) Subjects with healed lymphatic or bone tuberculosis marry with personal impunity and may beget healthy children. It is undeniable, however, that in such families scrofula, caries of the bone, arthritis, cerebral and pulmonary tuberculosis are more common. Which is it, "hérédité de graine ou hérédité de terrain," as the French have it—the seed or the soil, or both? We cannot yet say. The risks, however, are such as may properly be taken.

(2) The question of marriage of a person who has arrested or cured lung tuberculosis is more difficult to decide. If a male, the personal risk is not so great; and when the health and strength are good, the external environment favorable, and the family history not extremely bad, the experiment—for it is such—is often successful, and many healthy and happy families are begotten under these circumstances. In women the question is complicated with that of childbearing, which increases the risks enormously. With a localized lesion, absence of hereditary taint, good physique, and favorable environment marriage might be permitted. When tuberculosis has existed, however, in a girl whose family history is bad, whose chest expansion is slight, and whose physique is below the standard, the physician should, if possible, place his veto upon marriage.

(3) With existing disease, fever, bacilli, etc. marriage should be absolutely prohibited. Pregnancy and parturition hasten the process in almost every case. There is much truth, indeed, in the remark of Dubois: "If a woman threatened with phthisis marries, she may bear the first accouchment well; a second, with difficulty; a third, never." (On this subject the monograph of Reibmayr, *Die Ehe Tuberculoser*, may be consulted with advantage.)

PROPHYLAXIS IN TUBERCULOSIS.

The measures directed to the prevention of tuberculosis may be considered under—first, those which are concerned with the destruction of the widespread germ; and second, measures directed to maintain the nutrition of the individual at its maximum.

General Measures.—(*a*) Disinfection of the sputum. The most common method of dissemination of the disease is with the expectoration of tuberculous patients. In a dried form it is spread broadcast with the dust, and every patient in the stage of cavity is a focus of danger. When one considers that such a patient may, as shown by Nuttall, expectorate, at a very moderate estimate, from two to four billions of bacilli in the twenty-four hours, the danger is by no means imaginary. The patient should be directed always to use a spit-cup or the handkerchief, and never to spit on the floor or on the ground. The sputum may be disinfected by thorough boiling or a solution of carbolic acid of the strength of 1 : 20 may be put into the spit-cup. The handkerchiefs used by the patients should be thoroughly boiled. It should be explained frankly to the patient that the risk practically is from this source alone, and the friends should be given to understand that with due precautions the danger of nursing and caring for a consumptive is *very slight indeed.* The patient should occupy a single bed in a well-ventilated, airy room.

In the advanced stages, when the diarrhœa is present, the stools should be carefully disinfected.

The disgusting habit of expectorating in public, which is so common in this country, should be tabooed, and in public conveyances, such as street-cars, should be strictly forbidden. It is no hardship to ask a consumptive to carry some convenient form of spit-cup.

As already mentioned, the public has already been pretty widely instructed as to the importance of care in dealing with tuberculosis. Hospital authorities and health boards could issue with advantage a leaflet such as that which Cornet has prepared, which reads as follows:

"*Protection from Consumption.*

"The most destructive disease of the human race is consumption (tuberculosis). It carries off a seventh of the population. In Germany alone there die yearly of consumption wellnigh 150,000 people.

"It has now been discovered that this disease is caused by the inhalation of a germ, a so-called bacillus. It is infectious—that is, it can be given by any person to another. But neither the breath nor the perspiration of the patient is at all dangerous, as used to be supposed. Infection generally takes place through the spit, and, according to the latest inquiries, especially when the spit is discharged by the consumptive upon the floor or in a handkerchief, where it dries and becomes dust, and some of the swarm of germs contained therein are inhaled by healthy people.

"Many other diseases, such as diphtheria, pneumonia, and various forms of catarrh, may be communicated in a similar way.

"Consumptives endanger not only those about them, but themselves, through the drying of their spit, because they again inhale the discharged and dried bacilli, and thus infect hitherto sound parts of their lungs.

"Such infection may be avoided if consumptives—and, indeed, all who have a chronic cough with expectoration—keep this expectoration

ays moist; if they give up spitting on the floor or into a hand-
chief, and always use a spittoon which is emptied down the water-
et.

‘Spittoons must be placed wherever necessary, in every enclosed
e frequented by men. They ought not to be filled with sand or
dust, but either left entirely empty or supplied with a very lit-
water. They ought to be at hand in sufficient numbers in every
artment of houses, in workshops and factories, in counting-houses,
hools, offices, public places, in corridors and on stairs, so as to give
ery one a convenient opportunity of observing these injunctions.

“In this way healthy people who have to remain within the same
oom as consumptives will be almost entirely protected from infection.

“Posters ought to be put up in factories, workplaces, etc. forbidding most strictly spitting upon the floor or into a handkerchief.

“On the street, where spitting can scarcely be prevented, certain other circumstances diminish the risk of infection.

“Let every man, even though suffering from an ordinary cough, discharge his spit, not on the ground, not in a pocket-handkerchief, but always in a spittoon.

“Milk ought, as far as possible, to be used only after boiling, especially by children, invalids, and convalescents.

“By the strict observance of these injunctions consumptives are made almost harmless to those about them; and all the more that the bacilli can live outside the body only for about six months, it may be hoped that, if these rules are followed out by the sick, consumption in general will diminish.”

(*b*) In large cities the health boards should be empowered to carry out certain regulations. The measures which have been adopted by the Board of Health at New York are not only extremely reasonable, but may be recommended to other cities as models to follow:

“1. The department will hereafter register the name, address, sex, and age of every person suffering from tuberculosis in this city, so far as such information can be obtained, and respectfully requests that hereafter all physicians forward such information on the postal cards ordinarily employed for reporting cases of contagious disease. This information will be solely for the use of the department, and in no case will visits be made to such persons by the inspectors of the department, nor will the department assume any sanitary surveillance of such patients, unless the person resides in a tenement-house, boarding-house, or hotel, or unless the attending physician requests that an inspection of the premises be made; and in no case where the person resides in a tenement-house, boarding-house, or hotel will any action be taken if the physician requests that no visits be made by inspectors, and is willing himself to deliver circulars of information or furnish such equivalent information as is required to prevent the communication of the disease to others.

“2. Where the department obtains knowledge of the existence of patients with pulmonary consumption residing in tenement-houses, boarding-houses, or hotels (unless the case has been reported by a physician and he requests that no visits be made) inspectors will visit the premises and family, will leave circulars of information, will instruct the person suffering from consumption and the family as to the measures which should be taken to guard against the spread of the disease, and, if it is considered necessary, will make such recommendations for the cleansing or renovation of the apartment as may be required to render it free from infectious matter.

"3. In all cases where it comes to the knowledge of the department that premises which have been occupied by a consumptive have been vacated by death or removal, an inspector will visit the premises and direct the removal of infected articles, such as carpets, rugs, bedding, etc., for disinfection, and will make such written recommendations to the board as to the cleansing and renovation of the apartment as may be required. An order embodying these recommendations will then be issued to the owner of the premises, and compliance with this order will be enforced. No other persons than those there residing at the time will be allowed to occupy such apartments until the order of the board has been complied with. Infected articles, such as carpets, rugs, etc., will be removed by the department, disinfected, and returned, without charge to the owner.

"4. For the prevention and treatment of pulmonary tuberculosis it becomes of vital importance that a positive diagnosis shall be made at the earliest possible moment, and, that the value of bacteriological examinations of the sputa for this purpose may be at the service of physicians in all cases not under treatment in hospitals, the department is prepared to make such bacteriological examinations for diagnosis, if samples of the sputa, freshly discharged, are furnished in clean, wide-necked, stoppered bottles, accompanied by the name, age, sex, and address of the patient, the duration of the disease, and the name and address of the attending physician. Bottles for collecting such sputa, with blank forms to be filled in, can be obtained at any of the drug stores now used as stations for the distribution and collection of serum tubes for diphtheria cultures. After the sputum has been obtained, if the bottle, with the accompanying slip filled out, is left at any one of these stations, it will be collected by the department and examined microscopically, and a report of the examination forwarded to the attending physician free of charge.

"5. The authorities of all public institutions, such as hospitals, dispensaries, asylums, prisons, homes, etc., will be required to furnish to the department the name, sex, age, occupation, and last address of every consumptive coming under observation within seven days of such time."

(*c*) *Inspection of Dairies.*—A certain proportion of cases of tuberculosis, particularly in children, are caused by the drinking of milk of tuberculous cows. Every dairy supplying milk to the city should be systematically inspected, and full power should be given to confiscate and kill suspected animals. Where this systematic inspection is not carried out the milk should be boiled.

(*d*) *Skilled veterinary inspection* should be made at the abattoirs of the carcasses of all animals. There is much less danger of infection through meat than through milk.

The widespread diffusion among the public of knowledge on the subject of tuberculosis will undoubtedly be very beneficial. Such societies as have been organized in Philadelphia for the prevention of the disease will do great good by teaching proper measures of protection against the disease and by influencing public opinion in the right direction. Many persons, even among physicians, regard it as a great hardship that a consumptive should be under the surveillance of the health board, but the measures required to be carried out in the interest of public safety are neither exacting nor irksome. Sanitarians, however, must not be content with such measures as are directed against the *seed* alone. In the larger cities, particularly those with narrow streets and high tenement-houses, these measures must be combined with others directed to improvement of the conditions under which many of the people live, particularly to obtaining clean, dustless streets and affording a maximum amount of fresh air and sunshine.

Individual Prophylaxis.—A mother with pulmonary tuberculosis should not be allowed to suckle her child. An infant born into a family in which tuberculosis has prevailed or born of tuberculous parents should be watched with special care, and guarded particularly against catarrhal affections of all kinds. The convalescence from the fevers of childhood, more particularly measles and whooping cough, should be watched with special attention. A frequent cause of impaired vitality in young children is the condition of the tonsils. On the first indication of mouth-breathing a thorough examination should be made for adenoid vegetations, which if present should be removed. If a child has also recurring attacks of tonsillitis and the organs are at all enlarged, it is best to have them cut out.

The child should be clothed in flannel and live in the open air as much as possible. The sleeping room at night should be well ventilated. It is a good practice for the mother to bathe the throat and chest of the child every morning with cold water. The meals should be at regular hours, the food plain and substantial, and the child should be encouraged to drink milk. Many children have when young an aversion to fats of all kinds, but they should be encouraged to take cream and butter and milk. If the child becomes anæmic or its health seems failing, cod-liver oil, the syrup of the iodide of iron, and arsenic are the best tonics. If the thorax is naturally long, narrow, and contracted, something may be done to improve the condition by systematic pulmonary gymnastics and regulated exercises. In the choice of an occupation preference should be given to an out-door life. Families with a marked predisposition to the disease should, when possible, reside in an equable climate.

TREATMENT OF TUBERCULOSIS.

(*a*) DIETETIC TREATMENT.—As the healing of a tuberculous process is largely dependent upon the state of general nutrition, the question of diet becomes of the very first importance. Persistent failure properly to digest food is an unfavorable feature in any case. The variations in this respect are remarkable. There are patients in whom the appetite and digestion are not disturbed in the slightest degree, and while, as a rule, these are the most hopeful subjects, even in such, in spite of active powers of digestion and assimilation, tuberculosis may make rapid progress. So soon as the disease is recognized the practitioner should emphasize to the patient and to the friends the necessity of the most careful attention to diet, and his instructions should be specific, not general.

In the initial stages, with irregular fever and irritative cough, there is loss of appetite, at times nausea or even a positive aversion to food. Care should be taken that this condition is not aggravated by cough mixtures, creasote, cod-liver oil, and hypophosphites with which the patient is too often at this period drenched. In the pronounced gastric irritability of the early stages it is best to confine the patient to a liquid diet, consisting of one of the milk preparations, with or without egg albumen and meat juices. The milk may be taken either raw, diluted with Apollinaris or seltzer water, or half an ounce of lime water is added to each glass, or it may be peptonized, though, as a rule, the disagreeable taste is very objectionable to tuberculous patients. Buttermilk, koumyss, or kefir sometimes agrees much better than the simple milk. When there is an insuperable objection to milk, the meat juices and scraped meat and meat cakes may be used, and these articles made from the fresh meat are to be much preferred to the beef peptonoids and other similar preparations on the market.

Eggs form a most important article of dietary in early tuberculosis. Patients are not always able to eat the yolk, but when the proper amount of milk is not borne the egg-white is a useful addition, and is usually easily digested. When there is much gastric irritability, a glass of hot water early in the morning, or in extreme cases lavage, will be found useful. It is rarely necessary to resort to Debove's method of forced feeding, in which, after lavage of the stomach, a mixture is given through the tube, containing a litre of milk, an egg, and one hundred grammes of very finely minced meat. A patient will sometimes take this three times a day without special disturbance. It is not often that one has to resort to rectal alimentation in the early stages of tuberculosis. When solid food can be taken a varied diet may be given, in which the albuminous elements largely prevail, and to which are added the more easily digested forms of vegetables. Usually four or even five light meals are better borne than three large ones. On a mixed diet the patient does not need so much milk, and if plenty of cream and good butter is taken it is well not to insist upon its use. These measures may prove of no avail whatever in the treatment of a case unless the patient's surroundings are favorable, and improvement in the digestion may not occur until he removes from home or begins an open-air life. As already mentioned, very special care should be taken not to aggravate the dyspepsia by medicines. As a rule, the bitter tonics, with acids, and the preparations of malt are well borne and are very useful.

In the later stages of tuberculosis the dyspeptic symptoms may again be the most troublesome symptoms to combat, and the patient usually does best upon the albuminous diet referred to above.

Alcohol should not be given as a routine matter to tuberculous patients. It is often beneficial in cases with feeble digestion and high fever and in the later stages of the disease, when the heart's action becomes rapid and weak. There are cases in which three or four ounces of whiskey, taken as milk punches or given with the egg albumen, seem to promote the appetite and improve the general nutrition. Routine inistration is not advisable, and there is no evidence to uphold the old that the persistent use of alcohol promotes fibroid changes in the rculous areas.

b) PULMONARY GYMNASTICS.—In incipient cases much benefit results systematically carried out forced inspiratory movements, which ease the chest capacity and favor particularly expansion of the es. The patient should be directed to draw slowly the fullest possi- inspiration, raising at the same time the arms above the head. At end of the act the breath may be held for a few moments. These rts may be repeated slowly for from ten to fifteen minutes, morning d evening. The practice should be carried out systematically, and ercurrent hæmoptysis or high fever should be alone regarded as con- indications. Sometimes pains in the side are produced at first, probly from stretching of pleural adhesions, but they usually disappear with persistence in the effort.

(c) CLIMATIC TREATMENT.—The essence of the treatment of tuberculosis by climate is a life in the fresh air. A majority of the unfortunate victims of tuberculosis live in small rooms in small houses, and even the outside air can scarcely be called pure; yet even in our larger cities it is at any rate *fresh* in comparison with the quality of the air breathed in rooms heated above 70° and with all possible avenues of ventilation closed. As a large proportion of all patients are unable to seek any change, the first duty of the physician is to see what can be done in the way of fresh-air treatment at home. The patient and friends must first be convinced of the necessity for fresh air and their minds disabused of the dread of catching cold. Even in small houses the sunshine reaches some rooms for a certain period of the day, and the patient should be covered warmly in the bed, the bed wheeled in the sunshine, and the windows opened widely. In other instances the patient may rest for hours on a couch on the veranda. Even in the winter months no degree of cold contraindicates this open-air life. With plenty of rugs and clothing this practice may be carried out even with the most delicate patients, who, as a rule, quickly learn to appreciate the benefit. The sleeping room should have a southern exposure, and if possible an open fireplace. The patient should sleep with the window partially open, and it is an easy matter even in small rooms to prevent any draught from blowing directly upon the bed.

In the comparatively limited number of persons who are able to leave their homes the doctor is called upon first to decide whether the patient is in a condition to travel, and second to choose the locality to which to send him. Patients with disease localized at one apex and without high fever or much constitutional disturbance can be sent away with advantage. Cases with rapid tuberculous consolidation, high and irregular fever, and rapid loss in weight are better at home until some lull takes place, or, at any rate, until there is some positive indication that the case is not one of *phthisis florida*.

With well marked cavities, hectic fever, night sweats, and progressive emaciation the physician should, when possible, resist the importunities of the patient and friends (which are often under these circumstances most urgent) and keep the subject at home.

In deciding upon a suitable climate there are many questions to be considered besides those relating directly to the disease, particularly the patient's circumstances, constitution, etc. The climatic treatment of tuberculosis is, after all, only the open-air plan under more favorable auspices. There are three requirements in a suitable climate: pure atmosphere, an equable temperature not subject to rapid variations, and a maximum amount of sunshine. Living an out-door life, it makes little difference where the patient resides if these factors are present.

The purity of the atmosphere is the first consideration, and it is this requirement that is so well met in the mountains and forests. Dryness of the air is a factor upon which perhaps too great stress has been laid. Colorado and parts of Mexico are ideal dry climates; for example, at Denver the total rainfall per annum is rarely more than fourteen or fifteen inches, and the relative humidity is also very low. That dryness, however, is not an essential factor is seen in the beneficial results obtained in certain health resorts, such as Torquay and Falmouth in the south of England, one of the most humid atmospheres in the world.

Altitude is a secondary consideration. The rarefaction of the air is of great benefit in certain cases, and the increase in the frequency and depth of the respirations and the changes in lung capacity and in the size of the chest are very beneficial, particularly in the early stages of the disease.

Equability of the climate is a factor of great importance. Sudden changes of temperature, particularly when combined with high winds, are very trying to consumptives. Low temperatures, formerly so dreaded in tuberculosis, have been found by the experience at the Adirondacks and at certain Swiss resorts to be beneficial. Practically, the division of Jaccoud into climates of low and of high level is the most satisfactory, the former being more sedative and soothing, the latter stimulating and invigorating. Of low level climates in Europe, the Riviera, Egypt, Algiers, and some of the resorts in the south of England are the most frequented—in America, the Bermudas, the West India islands, Florida, and the coast of California. They are most suitable for cases of advanced tuberculosis with fever, for those cases in which the softening is progressive, for the subjects of chronic fibroid tuberculosis with emphysema, and for patients with the severer complications, as tuberculosis of the larynx and the intestines. Many of the most beneficial of these comparatively low level resorts are inland, and in this country Aiken in South Carolina and Thomasville in Georgia are examples of warm dry climates which prove very beneficial in many cases of tuberculosis.

The high altitudes are particularly beneficial in the early stages of the disease, before cavity formation or before extensive consolidation have occurred, and when there is not much fever. Chronic cases with hectic fever, extensive disease at both apices, great cardiac irritability, emphysema, and serious complications, laryngeal or intestinal, are unsuited to high altitudes. Many of the most favorable of these resorts have only medium altitudes, from 1500 to 3000 feet. Such in Europe are the well known resorts of Falkenstein and Goerbersdorf and in this country the Adirondacks and Asheville. Of resor
high altitudes, from 3000 to 7000 feet, in Europe Davoz Pl

Saint-Moritz, and in this country Colorado, are the best known. Cases of early tuberculosis, as a rule, do well either in the medium or high altitudes, and unquestionably one finds a larger percentage of arrest of the disease in the subjects who have gone early either to the Adirondacks or to Colorado than among those who have gone to the low level climates. From a medium altitude, such as the Adirondacks, a patient after a residence of two or three years may return with impunity to the sea level. In a majority of instances the patient who goes to Colorado must make up his mind to live there. A permanent return to the sea level is rarely practicable, and recurrence of the disease not infrequently follows the attempt.

(*d*) TREATMENT IN SANITARIA.—For many years special hospitals for pulmonary tuberculosis have existed, but of late the attention of the profession has been called to the great advantage of the treatment of the disease in institutions in country districts especially suited to the purpose.

In Europe the sanitaria of Falkenstein and Goerbersdorf are the most celebrated. The former, founded by Dettweiler, is situated in the Taunus Mountains at a height of 400 metres above the level of the sea. The climate does not differ in any respect from that of Central Germany, but the air is pure and free from dust and moisture. The institution is in the hands of a company and has been very successful. The out-door treatment is raised to a system, and it is stated that the number of patients confined to their rooms is only about 8 per cent. in the summer and 9 per cent. in the winter.

The sanitarium at Goerbersdorf in Silesia, founded by Brehmer. has accommodation for 250 patients, and in it, too, is carried out in a systematic, rigid manner the open-air treatment of the disease. The results in both of these institutions are remarkable. Recent statistics, as given by Knopf,[1] show a recovery of about 25 per cent. and an improvement in from 45 to 50 per cent. In this country the Adirondack Cottage Sanitarium, now in the twelfth year of its existence, has proved, under the management of Trudeau, a model institution of its kind. It has now a capacity of 74 beds, a certain number of which are free, and in others the rate is such as to be within the reach of persons with moderate means. Of 91 patients who remained from three to forty-four months, the average residence being ten months and twenty-five days, 19 cases were apparently cured; in 31 the disease was arrested; in 22 the condition was improved; in 18 there was no improvement; and 1 patient died of tuberculous peritonitis.

The Saranac Sanitarium is not only an object lesson of the greatest value in showing how much may be done for the relief of tuberculosis in a properly arranged institution, but it also demonstrates how the scientific study of tuberculosis may be carried on. The good example set at Saranac has been followed in other places, and the Sharon Institution in Massachusetts, under Vincent Bowditch, has also shown how much may be done in a similar way with less favorable climatic surroundings. We may look forward within a few years to a rapid advance of this method of dealing with tuberculosis. (For further information with reference to sanitaria the reader may consult the essay of Knopf, already referred to.)

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[1] *Les Sanataria: Traitĕment et Prophylaxie de la Phthisie pulmonaire*, Paris, 1895.

These sanitaria are largely for the treatment and care of pay patients, but in time cities will arrange for public institutions in suitable localities not far distant, to which cases of early pulmonary tuberculosis can be sent for systematic treatment. The civic health board will in future provide for two classes of pulmonary tuberculosis—the early curable cases, which will be sent to sanitaria, and the chronic, incurable cases, which will be cared for in well conducted hospitals in the immediate vicinity of the city.

(*e*) GENERAL MEDICAL TREATMENT.—So far as we know, there are no agents which have a special and peculiar action on the tuberculous processes. The chief remedies employed against the disease influence the general nutrition, increase the normal physiological resistance, and perhaps render the tissues less liable to invasion. The following are among the most important remedies which act usefully in this way:

Creasote and its Derivatives.—Under the use of these preparations many tuberculous patients increase in weight and present a general amelioration of the local symptoms. The best beechwood creasote should be used, given either in pill form or in capsules, alone or, as Sommerbrodt recommends, with cod-liver oil. If the pills and capsules disagree, it may be given in a solution with tincture of gentian, alcohol, and sherry wine. Sometimes the carbonate of creasote is better borne by the stomach; as it contains over 90 per cent. of creasote, the dose is the same. The good effects of creasote depend very much upon the amount the patient is able to take. One rarely sees such good effects from the small doses, though it is well to begin with a couple of minims twice a day. Patients who are tolerant of large doses do better, and ten, or fifteen, or twenty minims, or even half a drachm, three times a day may be taken. If, as is only too frequently the case, the drug disturbs the stomach, it may be given by the rectum as an emulsion with oil and egg. Other methods are by inhalation and subcutaneously.

Of derivatives of creasote, *guaiacol* is the one which has been most frequently used. It may be administered in pearls of one or two minims three times a day, or it may be given hypodermically in doses of one minim in olive oil, and is very often for this purpose combined with iodoform. The carbonate of guaiacol may be substituted in doses of from three to five grains.

Creasote has no direct action on the tubercle bacilli, but under its use in some cases the cough lessens, the expectoration diminishes, the sweats disappear, and the general nutrition improves. It constitutes the least unsatisfactory drug in the treatment of the disease.

Arsenic influences very favorably the nutrition, and may be used in doses of from three to five minims of Fowler's solution three times a day, increasing if it is well borne. In pill form, in doses of from $\frac{1}{75}$ to $\frac{1}{50}$, increasing up to $\frac{1}{12}$ of a grain, it is less apt to disturb the stomach. Patients who can take large doses for a considerable period of time are sometimes much benefited.

The *hypophosphites*, of which various preparations are on the market, are useful as general tonics. They have no specific influence upon the tuberculous processes. The hypophosphite of lime and the syrup of the iodide of iron are sometimes found useful in combination.

Cod-liver oil is useful in many forms of tuberculosis. It acts better in children than in adults. It may be given in teaspoonful doses three or four times a day. When well borne and assimilated its use is often followed by a marked improvement in the general condition. In an emulsion with hypophosphites it is sometimes better borne. In the glandular tuberculosis of young children it seems particularly beneficial.

Iron is useful in the anæmia of tuberculosis under certain conditions. When much fever is present or when digestion is greatly disturbed it is useless, but in the chloro-anæmia of the early stages there is no remedy more valuable. Great care must be taken not to disturb the stomach, particularly with the stronger preparations of iron. Children usually take the syrup of the iodide of iron readily.

(*f*) TREATMENT OF SPECIAL SYMPTOMS IN PULMONARY TUBERCULOSIS.—(1) *Fever.*—No single condition in tuberculosis is more difficult to combat than the pyrexia. When high and persistent the patient should be *at rest*, and when practicable in the fresh air and sunshine for a considerable part of each day. Sponging with tepid water will be found beneficial. Drugs are most unsatisfactory. Quinine, digitalis, and the salicylates may be tried, and the combination of the two former drugs is sometimes followed by good results. Antipyrine and phenacetin, if used at all, should be employed with caution, as in full doses both these drugs are apt to cause much depression. The external application of guaiacol, fifteen to twenty-five minims, rubbed on the skin, is often followed by a prompt but transient reduction in the fever.

(2) *Sweating.*—This is frequently associated with the fever, particularly in the later stages of the disease. It may occur independently as a result of exhaustion. The sweating is usually most distressing at night and in the early morning hours. Sponging at half-past nine or ten in the evening with tepid or cold water will sometimes reduce the temperature and prevent the sweating. Of the few trustworthy remedies for this symptom, atropia heads the list. It may be given in doses of from $\frac{1}{150}$ to $\frac{1}{60}$ of a grain. It often has an unpleasant effect in drying the mouth. Aromatic sulphuric acid, alone or in combination with gallic acid, is sometimes beneficial. When the sweat seems to be induced by the cough, opiates are indicated. Of the scores of other remedies suggested for night-sweats few are efficacious.

(3) *Cough.*—The patient should be instructed to restrain the cough as much as possible. The irritative cough of the early stages of the disease is best treated with codeine in doses of from one sixth to one third of a grain. When more severe morphine may be necessary. Sometimes the combination with dilute hydrocyanic acid is very beneficial. When the cough is associated with much expectoration, particularly in the morning, it is best treated by warm alkaline drinks, taken immediately on waking, warm milk and Apollinaris water, to which has been added a pinch of salt and bicarbonate of soda. Inhalations of creasote, terebene, or the oil of eucalyptus are very serviceable in reducing the amount of catarrh. Some of the most distressing forms of cough rise from the laryngeal irritation, and for such local treatment is indicated.

(4) *For the diarrhœa* of chronic phthisis and of intestinal tuberculosis large doses of bismuth are useful, combined with Dover's powder. Enemata of starch and laudanum may be tried or the acetate of lead

and opium pill. In other instances the acid diarrhœa mixture, containing in each dose ten to twelve minims of the dilute acetic acid, one eighth of a grain of acetate of morphia, and a grain of the acetate of lead, may be tried. It is usually impossible to arrest the diarrhœa of the late stages of the disease. The effect of different forms of diet should be watched.

(5) *Laryngeal and Pharyngeal Complications.*—Persistent local treatment may do much to relieve the very distressing symptoms of advanced disease of these parts. Krause, Heryng, and others have called attention to the great importance of active local treatment directed to the healing of the deep ulcers and the radical removal of the tuberculous tissues. The remarkable results which have been obtained would indicate that we have been altogether too timid in dealing with these lesions. While laryngeal tuberculosis may in rare instances heal by general and climatic treatment, in a large proportion of all cases the condition is progressive, and when extensive and severe the cause of the most distressing symptoms to the patient. Heryng's results should stimulate laryngologists to more radical and thorough treatment of the disease.

(6) *Hæmoptysis.*—Early in the disease the bleeding comes from small erosions on the mucosa of the smaller bronchi or from areas of softening which have communicated with the bronchi; in the later stages the blood comes from eroded vessels in a rapidly softening caseous area, or from a vessel on the wall of a cavity, or, most common of all in the stages of cavity, from a rupture in a small aneurysm. The first indication is to quiet the action of the heart by rest, mental and bodily, and for this the soothing influence of morphine, which, as has been said, not only favors mental but vascular serenity, is very beneficial. If the patient is vigorous and robust and the bleeding should persist, venesection may be practised. It was a method resorted to frequently enough by the older practitioners. Sterne somewhere mentions that he was bled from both arms for bleeding at the lungs. Huggard of Davoz has recently recommended the renewal of the practice. An ice bag may be placed over the chest. Among measures which may lessen somewhat the amount of blood in the pulmonary circulation are the nitrites, which relax particularly the systemic arterioles. Small doses of salts or fractional doses of calomel may be administered to divert the blood to the portal system. Hot foot-baths may also be used. It is doubtful if any drug has a special influence in controlling hæmoptysis. Ergot is probably contraindicated, as it is stated to produce a distinct rise in the pulmonary pressure. Aconite, on the other hand, lowers the pressure, and if there is much vascular excitement it may be used. Aromatic sulphuric acid, tannic acid, lead, and gallic acid are warmly recommended.

(*g*) LOCAL TREATMENT OF THE LUNGS.—Many substances have been employed for direct injection into the lung tissue, of which creasote, a 3 per cent. solution in almond oil, carbolic acid, a 2 per cent. solution in glycerin, and iodoform in olive oil, are the most important. The good effects which surgeons have had in the treatment of joint tuberculosis with injections of iodoform suggest that a further trial be given to this remedy directly injected into the affected areas. In a few instances the cavity in pulmonary tuberculosis is so favorably situated that it could be laid open and drained.

One or two other special methods of treatment of pulmonary tuberculosis remain for consideration.

The use of *compressed air* in the pneumatic cabinet, which was so much in vogue a few years ago, has still a few warm advocates, and meets certain indications in those who cannot go away or who cannot live an open-air life.

Tuberculin.—The announcement by Koch that he had obtained a material which exercised a specific curative action upon tubercle caused a furor of excitement never, perhaps, equalled in the history of medicine. At present we are deep in the reaction following the failure to substantiate this claim. Tuberculin is a product of the growth of the tubercle bacilli, extracted with glycerin. Its use has been almost entirely abandoned. A few enthusiastic observers still claim to get good results, and good clinical physicians state that in suitable cases it may be used without risk. If employed, the dose should be small, not enough to produce fever. As a diagnostic means it is of the greatest value, particularly in the tuberculosis of cattle, and is probably of equal importance in man, in spite of the fact that the reaction sometimes follows in actinomycosis and leprosy.

Serum-therapy.—The blood serum of animals, particularly of dogs, goats, horses, and asses, which have been treated with the toxins of the tubercle bacilli is now used extensively in pulmonary tuberculosis. The employment is at present largely empirical. Maragliano in Italy claims the most remarkable results, and in this country Paquin of St. Louis has introduced the method, using the blood serum of the horse. I have no personal experience with the treatment, and from the reports which have been published it is not possible to speak with any confidence of the results.

In speaking of the treatment we have considered chiefly that of pulmonary tuberculosis, the most important form. In the tuberculosis of other organs the same general measures are to be carried out; the reader will find the local treatment referred to under the special sections.

NOTE ON TREATMENT OF TUBERCULOUS PERITONITIS.—The general hygienic and dietetic measures are to be carried out. Creasote, arsenic, cod-liver oil, and the hypophosphites may be used. Local treatment is sometimes advantageous. The tincture of iodine frequently applied often relieves the pain, and some have recommended mercurial inunctions. For the constipation which is so common mild laxatives should be used. Surgical procedures are of great value. In the ascitic form repeated aspiration may be practised. Laparotomy offers in certain cases the hope of cure, while in others relief may be obtained. The best results have been obtained in the ascitic form or in the localized peritonitis with encysted exudation. Where there are large nodular masses and evidence of the coexistence of extensive tuberculosis in other organs the conditions are not favorable.

SYPHILIS.

BY W. F. ROBINSON, M. D.

DEFINITION.—Syphilis is a chronic infectious disease, of long duration and irregular course, produced by a specific virus capable of attacking any and all tissues of the body. The disease manifests itself in a multitude of phenomena having their origin for the most part in an indolent inflammatory process accompanied by a new cell formation of low grade. It is acquired by inoculation with the blood or morbid secretions of an individual suffering with the malady, or is transmitted from the parent to the child. Persons once affected with syphilis are usually immune thereafter.

NATURE AND COURSE OF SYPHILIS.—Syphilis is a distinct and independent malady related etiologically in no wise to any other form of disease. No one today doubts the unicity of the infecting virus or that local infection with such virus will invariably be followed by systemic invasion and the development of true syphilis. The contentions of the dualists are ended and their fallacy is now only an interesting chapter in medical history. But no one as yet knows positively just what the infecting virus of syphilis is. It is unique in that it has thus far defied the most skilful and untiring investigators to unravel its complexity or determine its true nature. While evading recognition, there are still facts enough in existence to make it reasonably certain that the causative agent is a bacterium and that syphilis is a germ disease. No other theory of its origin will explain the symptoms manifested in its course so well as this. It seems certain also that the isolation and detection of the specific element cannot much longer be delayed.

Syphilis is a disease that is acquired either by inheritance or by infection of a sound individual with the virus as it comes from a person suffering with the malady. The first form is known as *Inherited Syphilis,* and the second as *Acquired Syphilis.* These two forms of the trouble differ from each other very materially in their course, their symptoms, and their gravity as relates to the life of the sufferer. The acquired form is a disease largely amenable to treatment and seldom imperilling the life of the individual affected, while the mortality in the inherited form is extremely great, and its mutilating effects are often made manifest in every tissue and organ of the body when life is spared.

The acquired form of syphilis is contracted most frequently in the contacts of sexual intercourse. It is because of this fact that syphilis is classed with and spoken of as a venereal disease. But syphilis is not always acquired in this manner. It is frequently contracted in ways other than by sexual congress. Kissing is often a source of infection; the use of toilet articles, towels, napkins, knives, spoons, pipe-stems, and cigar-holders previously contaminated with the virus of syphilis by persons suffering with the disease is a fruitful source of the malady; the breast of a healthy nurse is infected by the syphilitic child; surgeons, physicians, and accoucheurs are infected in the practice of their professions and in turn infect others in like manner. In all these ways and in many others syphilis can be transmitted. Syphilis acquired in a manner dominated by no erotic element is spoken of as *syphilis insontium,* or syphilis in the innocent. Its course differs in no wise from that pursued by the disease when acquired in the venereal act.

The contagium of syphilis cannot be carried in the air: it needs a more substantial vehicle. The easiest and most usual form of transmission is by direct and close contact with an individual suffering with the disease. If the conditions are favorable, there is then a direct passage of the virus from the unsound to the sound individual. Such method of acquiring the disease is said to be by *immediate* infection. When the virus is transmitted by means of some intervening carrier the infection is said to be *mediate.* In order that the virus shall make its entrance into the system it must be brought into contact with some solution of continuity in the skin or in contact with the mucous surfaces. It cannot make its way through the sound integument. The break in the skin may be exceedingly minute; it may be the merest abrasion or pin-point opening, but it is always there as an open door through which the poison may enter. Upon the mucous and pseudo-mucous surfaces there is good reason for believing that such opening is not so necessary. Here the virus, if implanted and allowed to remain undisturbed, can make its way through the moist epithelial coverings to the tissues beneath. This it can do the more easily if it finds its way into a mucous or sebaceous follicle.

If pus infection of the wound does not take place at the time that the syphilitic virus is deposited, the wound closes and the parts appear unaffected. In this condition they remain for a variable length of time, usually about three weeks. This time, in which there are no manifestations of any trouble whatever, is known as the *first period of incubation.* Then the first symptom of syphilitic infection makes its appearance. This is in the form of a sore at the exact point where infection took place. This sore is known by various names, as the hard chancre, initial sclerosis, or initial lesion of syphilis. While this first lesion of syphilis is always strictly circumscribed and definite in its site, it is not true that the virus of the disease is entirely localized within it. At least partial invasion of the system has taken place before its appearance. Extirpation of the chancre does not abort nor in any way modify the course of the disease.

The chancre assumes variable and characteristic forms, to be described later. It usually follows a sluggish, indolent course, lasting from a few weeks to several months, and then, if it has been uncomplicated by pus infection, disappears completely, leaving no relics of its existence behind. At about the time that the chancre appears characteristic changes take place in the neighboring lymphatics and glands. These enlarge, become indurated and hard, but are seldom painful and rarely suppurate. They constitute the *bubo* of syphilis.

With the appearance of the chancre begins the so called *second period of incubation*. This period is ill defined and indefinite in its extent. It is made to include the development of the chancre, the enlargement of neighboring lymph glands, and that series of changes which takes place within the system before the appearance of eruptions on the skin. During this time the patient may retain the full vigor and appearance of health, or there may be prodromal symptoms, such as malaise, inappetence, headache, slight muscular pains, and occasionally a low or high temperature, showing that the system is slowly being brought under the influence of the poison. Then follows the first exanthem, and with its appearance the establishment of syphilis within the system is complete.

Up to this time the course of syphilis is reasonably certain and unvarying in different individuals. There are about the same changes and they occur in about the same succession, differing only in the length of time occupied in their evolution and development. After the appearance of lesions upon the skin and the thorough invasion of the body no such orderly succession of symptoms can be predicted. The trouble may end at once; it may become quiescent for a time and then break out with added intensity and vigor; it may go through a series of changes increasing in energy and variety of expression until it expends its force and then subsides; or it may enter at once upon a malignant and destructive course in which the integrity of various organs may be involved or life itself threatened.

Syphilis is a constitutional disease always. The involvement of the system may be severe, or it may be so light as to give rise to scarcely appreciable symptoms. Limitation of all symptoms to the chancre means that the systemic manifestations have been mild and the skin affections overlooked, or that the nature of the local lesion presented was misunderstood. Syphilis is a chronic disease, persisting usually for a long period of time and seldom presenting symptoms that can be classed as acute. Under favorable and early treatment most cases recover in from two to four years. Some cases are so mild that all symptoms vanish after the expiration of a few months, and never reappear. This happens at times with no treatment at all or that only of the most indifferent nature. In other cases the symptoms are severe from the beginning. Bone and brain lesions appear with or precede the skin eruptions. The skin may be quickly filled with ulcerating gummata instead of the more frequent macules and papules. The integrity of every organ in the body may be threatened and a fatal ending may ensue. This malignant form of the disease is called by the French "galloping" or "lightning" syphilis, and the terms are apt and appropriate. It is fortunate that such cases are rare.

Stages in Syphilis.—Ricord divided the course of syphilis into three periods, designating them, respectively, the primary, secondary, and tertiary stages. The primary stage began with the appearance of the initial lesion and continued until the development of generalized skin eruptions. The skin eruptions ushered in the secondary stage. This was more indefinite in course and extent, but was made to include the exanthemata occurring in the course of the disease, loss of hair, affections of the nails, sore throat, and mucous patches within the mouth cavity and elsewhere upon the mucous surfaces. The tertiary stage followed the secondary, and was still more indefinite in its course. It was supposed to begin at about the end of the first year and to continue until the termination of the disease. This classification, while of great service in the past, is not now regarded with the favor once accorded it. Its errors are becoming more apparent every day, and the time is not far distant when it will be entirely discarded. Its chief fallacy lies in the fact that it endeavors to make syphilis conform to a time schedule and a regular, unvarying succession of changes. Such a course syphilis does not pursue, and any attempt to make it appear that it does is misleading in the extreme. The tertiary stage in many cases never makes its appearance, all symptoms of the disease ending with the termination of the skin eruptions. Again, the secondary stage, as far as any of its chief manifestations are concerned, may be wanting entirely, and so called tertiary symptoms follow close upon the appearance of the chancre. The primary stage is the only one described by Ricord in which the symptoms are possessed of sufficient constancy and definiteness to warrant their being grouped as belonging to one period of the disease.

Syphilis must be recognized as a disease not following any one definite course and manifesting itself in a series of symptoms appearing at a certain time after the development of the chancre, these running their course within specified and exact limits, then to disappear and be succeeded by another set of symptoms equally clear and concise; but as a disease that, starting from a fixed point, pursues many different lines of evolution and expresses itself in a great variety of symptoms. Only in such manner can an intelligent conception of the malady be obtained.

ETIOLOGY.—The belief is wellnigh universal among scientific and medical men that syphilis is caused by a living germ. So many of the clinical facts and manifestations of the disease can be given a ready and satisfactory explanation by the assumption of such an hypothesis that the evidence is overwhelmingly in its favor. Moreover, reasoning from analogy, we are able to reach the same conclusions. Syphilis undoubtedly belongs to the infectious granulomata. Its infectiousness, the course it pursues, the development, structural anatomy, clinical appearances, and ultimate termination of its various lesions are all in accord with diseases of this class. In this group of affections are included leprosy, tuberculosis, glanders, lupus vulgaris, mycosis fungoides, and actinomycosis. All of these diseases are known to be inoculable; bacteria are found constantly in their lesions; and in some, as in tuberculosis, glanders, and actinomycosis, certain of these organisms are positively known to be the causative agent in their production. These facts furnish good evidence for our belief that syphilis originates in the same manner.

While the existence of a bacterium that produces and perpetuates syphilis is highly probable, its detection, isolation, and thorough demonstration have not yet been accomplished. In 1884, Lustgarten described a bacillus which he had found in syphilitic tissues and which he believed to be the microbic element of the disease. The bacillus was from three

o seven micromillimetres in length, or about the size of the tubercle
acillus, had a slightly curved or S-shaped appearance, and had knob-
ike enlargements at its ends. Since making his investigations other
bservers have verified the existence of the bacillus in tissues of like
ature.

These bacilli have been found in the tissues and secretions of chancres
d moist papules, in dry papules, mucous patches, gummata, condy-
mata, and lymph glands. They are not numerous, usually being found
ne or in groups of two to eight within cells somewhat resembling,
t larger than, white blood corpuscles. They occur most frequently
r the advancing border of the lesion, rarely deep within its substance.
The staining method employed in their demonstration is briefly as
ows: Thin sections of the part to be examined are made through
border of the lesion, including, if possible, sound as well as syphi-
tissue. These sections are placed in a solution consisting of
parts of aniline water, and 11 parts of a concentrated alcoholic
ion of gentian violet. In this they are allowed to remain for
ty-four hours. Then the temperature of the solution is raised to
. and the immersion is continued for two hours longer, after which
ctions are removed and placed in absolute alcohol for five min-
On removal from this they are dipped for ten seconds in a 1½
nt. solution of permanganate of potassium, and are then decol-
in sulphurous acid largely diluted with distilled water. If after
ough attempt it is seen that decolorization of the specimen can-
completely effected, the process of washing in alcohol, perman-
solution, and a stronger solution of sulphurous acid must be
d. The section when ready for mounting must be colorless to
ed eye. When decolorization is complete the section is washed
lled water, cleared in the usual way with oil of cloves, mounted
rin or Canada balsam, and examined with a $\frac{1}{12}$ inch oil immer-
s.

acillus thus described may be the active causative agent of syph-
enough has not been done as yet to prove it such. Lustgarten
carry his work to completion, nor has any other investigator
ince. It is not enough to find certain forms of bacteria present
hilitic tissues. They must be found constantly in all at least
lier lesions. They must be removed from such lesions, isolated
ther species of bacteria, and pure cultures must then be made
ble media. From these cultures inoculation experiments upon
free from any taint of the disease must be made, with the
roducing in them demonstrable syphilis. In the lesions of
s produced the same germs must be found. These are essen-
's laws, and in the round that they require can complete
be obtained. Only when this shall have been accomplished
cillus of syphilis be completely demonstrated. One great
the way of demonstrating the germ of syphilis is the fact
are immune to the disease. Inoculation experiments have
peatedly upon them, but only in rare instances with in-
ess. The help afforded in the study of tuberculosis by
re denied.

.—Syphilis is a disease that expresses itself in a great variety of ways and with a multitude of symptoms. Frequently it expends its entire energy in an attack on one organ or one set of organs. Thus the symptoms may be confined entirely or in large part to the skin, to the bones, to the nervous system, or to any one of the various organs or systems of organs of which the body is composed; or a number of organs may be attacked simultaneously or in succession. Again, in its encroachment upon a given organ it is not by any means uniform in the lesions that it produces or the effects to which it gives rise. There is no lesion of the skin known to the physician that syphilis may not reproduce, and in its involvement of deeper structures it furnishes nearly as extensive a list of pathological phenomena. Hence the study of symptoms presented by syphilis must be a study of its different lesions and their varying expression in different organs.

The First Period of Incubation.—After the syphilitic virus has gained entrance to the system an interval occurs in which there is no appreciable evidence of infection. This interval occupies a period of time varying from ten to thirty days. At the expiration of this incubative period the hard chancre or initial sclerosis makes its appearance at the point where infection took place. The length of this incubative period varies within quite wide limits. Ten days appears to be the shortest time on record in which the date of infection was indisputable, while periods as long as sixty and seventy days have been noted by careful observers. Very long or very short periods are exceptional, however, and always open to suspicion. The great majority of chancres occur at about the end of the third week.

The point at which the chancre is situated is always the point where contamination with the syphilitic virus has taken place. Infection never occurs at a distance from this point. Two or more points may, however, be infected at the same time, and if this occurs there will be an equal number of chancres resulting. Thus it may happen that a man may get a chancre of the lip at the same time with a chancre of the penis, the one acquired by kissing, the other by coitus with the same woman. But this is unusual.

During this incubation period it is highly probable that the virus does not remain localized and latent, but that it undergoes distribution with developmental changes too delicate for our coarse methods of appreciation. Certain it is that infection of the system occurs within a relatively short period of time after contamination has taken place. This is shown by the fact that if an abraded surface or open wound through which the poison is supposed to have passed be thoroughly cauterized or deeply extirpated within a few hours after inoculation has taken place, it does not in any wise affect the appearance of the chancre or the course of the subsequent syphilis.

Chancre.—A chancre is that changed condition of the normal or unsound skin or mucous membrane produced by infection with the virus of syphilis, and occurring at the point where such infection has taken place. It is characterized by a varying degree of induration and an accompanying enlargement of the neighboring lymphatic glands.

Better and less confusing terms for its designation are the "initial sclerosis" and the "initial lesion" of syphilis.

The initial sclerosis does not occur in hereditary syphilis, and is never wanting in the acquired form. It may be so slight in its manifestations as not to attract the patient's attention, or it may be hidden deeply beyond the external openings of the body, such as in the mouth cavity or vagina, and thus escape detection, but its existence is none the less certain. Cases of syphilis in which it is declared to have been absent are simply cases in which it was overlooked or misunderstood. It is one of the few symptoms in syphilis that is constant and unvarying in its appearance.

The initial lesion is the first symptom of syphilis to declare itself after infection, and it is also the first conclusive proof that infection has taken place. The site of its appearance is always definite. It occurs at the point or points of infection, and in no other localities. It is usually single, but if there has been coincident infection at two or more points, there will be a corresponding number of initial lesions. This frequently happens on the glans or foreskin when the rupture of a number of herpetic vesicles has opened different passageways for the entrance of the specific virus. Here as many as a dozen or more distinct and individual lesions may occur, each presenting the typical characteristics of a hard chancre.

The chancre of syphilis is not auto-inoculable. Its virus can be deposited upon the broken skin or mucous membranes of the individual upon which it occurs, and no chancre will result. In this it differs from the chancroid, which can be freely inoculated at different sites upon its bearer. When the chancre appears upon a surface that is brought constantly in contact with an opposing surface, it is apt to produce a lesion that looks as if auto-inoculation had taken place. This happens frequently upon the inner surface of the foreskin and the glans penis or between the lips of the vulva. If such secondary lesion be examined carefully, it will be found to be superficial, not at all indurated, and perhaps slightly ulcerated. It is caused by the irritation produced by the chancre, and not by any specific action of the syphilitic virus. No mistake need occur if careful examination of all lesions presenting themselves be made.

Sites.—As syphilis is acquired most frequently in the contacts of sexual intercourse the initial lesion is found oftenest upon the genital organs.

In the male it occurs upon the glans penis, in the sulcus coronarius near the frænum, upon the inner or outer surface of the foreskin, on the skin of the penis or scrotum, and at the meatus urinarius or deep within the urethra.

In the female the parts oftenest attacked are the labia majora and minora, the fourchette, the preputial covering of the clitoris, the entrance to the vagina, the os uteri, the perineum, and the inner surface of the thigh.

Other parts of the body where chancres may be met with are the lips, tip of the tongue, the tonsils and walls of the pharynx, the nipples and breasts in nursing women, the base of the nail and finger tips in surgeons, physicians, and accoucheurs, the lobe of the ear, the parts about the eye, and the umbilicus. In short, any part of the body where a break in the overlying structures may occur, and to which the virus of syphilis can be carried, may become the seat of chancre. **Chancres** occurring upon the genitals of either sex are spoken of as *genital chancres*, while those occurring elsewhere upon the body are known as *extragenital*.

All chancres have at least three determining features in common. These are—the period of incubation already described, a peculiar thickening and hardening in and about the lesion known as induration, and a characteristic enlargement of the lymphatic glands in the near neighborhood. These features are constant and diagnostic.

Induration.—Induration, in its degree and extent, differs very much in different chancres according to their anatomical location and the amount of external irritation to which they are subjected. The thickening may involve only the base of the lesion, seeming to the touch like a bit of parchment set within the tissues, or it may produce a mass the size of a marble and varying in density from that of cartilage to bone. The induration frequently can be detected at the outset, or, if inappreciable then, will usually make itself apparent within a few days. It continues to increase for a period varying from ten to fifteen or more days. At times the occurrence of induration is deferred somewhat longer, but it never fails to show itself. If the thickening be slight, it may disappear entirely before the chancre heals, but if extreme it usually disappears slowly. Some trace of it can often be discovered at the time of the first macular exanthem unless this be much delayed. Occasionally it persists for longer periods, as for six and eight months.

Bubo.—The accompanying glandular enlargement is known as syphilitic bubo. When the chancre is situated upon the penis, the bubo exists in both groins. It is said at times to be one-sided, when the chancre is not situated near the median line. This statement, however, needs confirmation. Enlargement upon one side only is of doubtful character. The glands are but slightly or not at all painful, and freely movable beneath the skin. They usually form in a series decreasing in size from the one nearest the chancre. In size they vary from that of a billiard ball to that of a hazelnut. The skin is not inflamed as in chancroid, and they rarely suppurate. Double inguinal adenopathy, with a characteristically indurated chancre appearing at the end of an incubative period of not less than three weeks, is sufficient to establish a diagnosis of syphilis. Treatment has a marked influence upon the duration and character of the bubo.

Form.—Chancres assume a variety of forms. They are frequently developed upon the site of pre-existing lesions, such as herpetic vesicles, smokers' patches, fissures, and excoriations, and take on certain of the features presented by such lesions. Anatomical location, pressure effects, friction, and treatment all tend to modify the chancre and in various ways determine the form that it shall take. No one lesion can be taken as the type of all chancres. Each must be studied by itself. Only the commonest forms can here be described.

Erosion.—This is the simplest type and the one most frequently met with. It appears as if a limited area of the epidermis or mucous membrane had been rubbed or scraped away. This form is frequently spoken of as the *chancrous erosion*. It is the primary form of the initial lesion, but with its simplicity it is the form that presents the greatest difficulties in the way of diagnosis. At the outset it is not much larger than the surface of a pinhead, is rounded or oval in outline, and appears as if the epithelium had been removed by friction with the clothing or opposing parts of the body. The eroded surface is on a level with the surrounding integument or but little depressed below it. Examination of its base usually shows a slight degree of induration, as if the lesion were resting on a bit of mica set in the skin. This may be wanting if the chancre is seen early, but it makes its appearance within a short time. During the evolution of the chancre the induration becomes well marked. The eroded surface remains diminutive in size, or enlarges by peripheral extension until it becomes as large as or larger than a ten-cent piece. The lesion is dark red or grayish in color. The surface has a glazed, velvety appearance, and at times is covered with a closely adherent pellicle looking somewhat like diphtheritic membrane. The base is bathed in a sticky serous exudate. This exudate can be made to flow freely by making gentle pressure at the sides or the lesion may bleed upon manipulation.

This form of chancre is usually single, but it may occur in numbers of a dozen or more. The minute eroded surfaces in such instances are grouped together, but each lesion is separate and distinct. The resemblance of such chancres to the lesions remaining after the rupture of a number of herpetic vesicles has given rise to their designation as "multiple herpetiform chancres." Early in their course they are exceedingly hard to distinguish from progenital herpes, but absence of itching and burning sensations should make the practitioner wary about committing himself to a positive diagnosis. Such chancres have a glazed surface not seen in herpetic lesions. Their tendency is to coalesce, forming a single large eroded surface.

When single the chancrous erosion sometimes assumes a cup-shaped depression with slightly elevated borders, or the floor may be lifted by the indurated base until it appears like an excoriated papule.

This form of chancre is found frequently in the male on the under part of the foreskin or in the sulcus coronarius. In those situations where it is protected from friction with the clothing or exposure to the air it finds the conditions suited to its best expression.

The induration may increase to such an extent as to give the chancre the form of a nodule varying in size from a pea to a marble and as hard as ivory. The erosion, often no larger than a pinhead and retaining its distinctive features, can usually be found upon the surface of this enlarged and hardened mass, or the chancre may heal and disappear while the nodule continues to increase in size. Nodular lesions of this kind are most frequently met with in the furrow back of the corona glandis. The abundance of connective tissue in this locality is favorable for such development.

The Dry Papule.—This form of chancre occurs in situations not subject to heat or moisture. The skin of the penis, the surface of the glans in men who have been circumcised, the pubic regions, and the skin of the body in general furnish favorable sites for its appearance. The papule begins as a reddened, indurated point not much larger than a pin-head, and increases slowly in size and elevation until it is several lines in height. The lesion is firmly indurated throughout, and the tissues at the base are more or less involved. The summit of at or convex, and is usually covered by a dry, somewhat t grayish scale. The papule is often surrounded by a reddened Its hue is dusky red or ham color. It may continue as a papule out its entire course or be converted into a pustule, and later te into an ulcer. Frequently after resolution a deeply pig- spot remains.

ule.—The pustular or ecthymiform chancre develops usually e dry papule. This type never originates primarily as a pus- ut is always secondary to some other form, and is due to infec- f such lesion with pus cocci. There is always a considerable of inflammation in and about the chancre, owing to the nature pus-producing elements. The roof wall soon breaks down, and stule becomes surmounted by a friable, yellowish or greenish crust. Considerable swelling of the foreskin is apt to occur he lesion is seated upon its surface or upon the glans.

r.—Chancres occur frequently in the form of ulcers. In all such ulceration is caused by friction, irritating discharges, un- liness, infection with pus microbes, or improper treatment. A ncrous erosion is often converted into a lesion of this type by the y and severe use of caustics. The ulcer may be either superficial or . When superficial the ulcer resembles the eroded form of chancre its early stages in that its base is not often deeply indurated. The er is shallow, has sloping walls, a raised or but slightly elevated der, and an unhealthy granular pus-secreting floor. In deep ulcers ulceration extends profoundly into the tissues, and the induration at the base and sides of the chancre exceeds that seen in any other m. This form of chancre is known as the "Hunterian chancre." ne walls are never perpendicular, but always slope gradually to the floor of the ulcer. The edges are raised, thickened, and intensely hardened. The secretion is purulent, and may be scanty or profuse. At times the lesion may be hemorrhagic and blood be mixed with the pus. The base of the penis overlapped by the pubic hairs, or the cruro-scrotal angle, is a favorite site for its development. Swelling and œdema of the penis are frequent accompaniments. Resolution is attended by loss of tissue and the production of a well marked cicatrix.

Chancres, as a rule, undergo complete resolution, leaving no trace of their existence behind, save perhaps a pigmented spot. When persisting until the development of skin eruptions they are frequently converted into lesions of a distinctly different type, the so-called moist papule or mucous patch.

Mixed Chancre.—This term is applied to those chancres arising from simultaneous infection with the virus of chancroid and of syphilis. The chancroidal elements are the first to develop. There is no incubative period, the sore appearing shortly after exposure. A pustule appears at the start. It is markedly inflammatory in its nature, and shortly becomes ulcerative. No induration can be detected at its base. If the sore appears upon the penis, a single gland in one groin may enlarge. Rarely enlargement occurs in both inguinal regions. The gland is tender to the touch, and soon becomes extremely painful. The skin covering it, is reddened and suppuration may occur.

After the usual period of syphilitic incubation has gone by the sore takes on new features. The base becomes hardened and the chancre assumes the characteristics of the ulcerative initial lesion of syphilis. There soon follows the multiple instead of single glandular enlargement, and systemic syphilis ensues.

Syphilis of the Skin.—Syphilis displays itself upon the skin of the individual suffering with the disease in a number of well defined and characteristic ways. It is usually here that the first positive proofs of systemic invasion are made manifest, and throughout the entire course of the malady the skin may show, in some portion of its extent, evidences of the disease. The lesions presented vary much in their nature, character, form, distribution, extent, and gravity of deportment. Those occurring early in the course of the disease are usually benign in nature and extensive in distribution, while those occurring at late periods are apt to be localized and destructive in their tendencies. The principal lesions exhibited upon the skin are in the form of macules, papules, pustules, ulcers, tubercles, and gummata, and they are called the syphilodermata. Early and exact recognition of these skin lesions is essential, because of the important help they furnish in establishing a diagnosis.

Macules.—These are the earliest of the syphilitic eruptions to make their appearance. They begin as slightly muddy discolorations of the skin, giving to the surface of the body a peculiarly mottled look. Often this condition cannot be seen with light reflected directly from the surface of the skin, but only when the light comes to the eye in an oblique direction. The eruption may come out slowly, ten or more days being occupied in the process, or it may develop rapidly, a single night sufficing for its complete evolution. This latter is more apt to be the case if the patient has recently indulged in a Turkish or other hot bath, by means of which the system has been overheated and the bloodvessels of the skin thoroughly relaxed.

In its complete expression the eruption is seen to consist of isolated macules, roundish or irregular in outline, from the surface of a split pea to a ten-cent piece in size, and of a pinkish or brownish hue. The color fades at first upon pressure, but later becomes more or less persistent. The eruption usually makes its appearance first upon the surface of the belly or of the chest, but it may occur in other locations, as the dorso-lumbar region or over the scapulæ and shoulders. The process if severe may extend over the greater part of the body surface. The face usually escapes, but when affected the process is seen in its best development at the base of the hair and over the brow. The eruption occurs almost constantly upon the palms of the hands and the soles of the feet. Examination of these regions should always be made in any case of suspected syphilis. The spots here show themselves as faint or well pronounced erythematous patches, circumscribed or ill defined in outline, and fading upon pressure. They may persist in this form throughout their entire course, or later develop into scaling papules. The dorsa of the hands and feet are far less frequently affected.

The macules in an early period of their development are usually unmixed with other forms of syphilitic lesions, but they may be readily transformed, if subjected to any form of irritation, into maculo-papules, in which there is slight elevation of the surface, and these be converted later into distinct papules. Occasionally they are commingled with pustules.

There is little or no sensation. If any is excited, it is evinced in form of a slight pruritus, which is seldom annoying. The patient ay not be aware when he presents himself for examination that his dy shows any traces of eruption. It should therefore be the rule enever practicable to examine the entire body surface. This should ays be done in the case of male patients, no matter at what stage of disease they may first present themselves. When not visible the ottling of the surface can be made to appear by exposing the skin for short time to a slightly chilly atmosphere.

In many cases the eruption is preceded by subjective symptoms, ch as malaise, inappetence, headache, and temperature varying from ghtly above normal to 102° or 103° F.

The eruption does not often persist for any great length of time. nder appropriate and energetic treatment it can be made to disappear a few days. Untreated cases may continue for a month or longer, t usually transformations of the lesions into papules takes place before e expiration of this period is reached, and the type of the disease is changed completely. Recurrence of the macular syphiloderm may take place at any time during the first year, but it is not often generalized. There is at these times a tendency on the part of the lesions to assume a circinate grouping.

There is usually some accompanying involvement of the mucous surfaces. Inspection of the throat shows hyperæmia of the pharynx, of the pillars of the fauces, and of the soft palate. Tenderness of the gums is also noticeable.

Resolution is usually complete, no relics being left to show the existence of previous trouble. But sometimes where the process has been severe more or less pigmentation may follow. This disappears in the course of time.

Papules.—Papules are among the commonest and most characteristic of syphilitic eruptions. They may appear at any time after the third month of the disease. Any part of the body surface may be affected. Frequently they appear in crops, and recurrence often takes place. They are discrete or in groups. Careful examination shows the groups formed in curved lines, circles or parts of circles, and S-shaped figures. Such grouping is pathognomonic. It is best seen over the abdominal and chest regions or upon the surface of the back. The papules vary in size from a grape seed to a split pea, or even larger. The large and the small varieties may be commingled in the same subject or be separate and distinct, a given individual showing but one form throughout the course of his disease. Rarely these small papules may be converted into the larger varieties. Occasionally they become pustules. They are many or few, conical or flat, moist or dry, and vary in hue from a light red to a dark ham color. Resolution is usually complete.

Papules may form the first eruption that appears upon the skin, or they may be developed with or directly follow the macular exanthem. They are best classified as dry and as moist papules.

Dry Papules.—Dry papules occur in two forms, known as the *miliary* and the *lenticular*. Miliary papules occur less frequently than do the lenticular. They are seen oftenest in uncleanly and neglected cases. For this reason they are seen more frequently in public than in private practice. Women exhibit them oftener than men. The papules are about the size of a pinhead, and when seen in their completest expression are thickly set over the entire body surface. There is usually no subjective sensation, but patients sometimes complain of slight itching or burning. The papules are conical in form, and the summit may be capped by a minute scale or be the seat of a tiny vesicle. Involvement of the hair follicle frequently occurs, and the papule is then pierced by the hair filament. Limitation of the miliary papules to exposed surfaces, such as the face and the hands, sometimes takes place, while the parts of the body protected by the clothing are the seat of much larger varieties. In cachectic and anæmic patients the appearance of a crop of miliary papules is often the precursor of an extensive pustular syphiloderm soon to follow.

Lenticular papules are the most frequently met with of any of the early syphilodermata. They are liable to occur at any time during the first two years after infection, and may appear at a still later period. They vary in size from a large pinhead to a coffee bean, have a flattened or rounded surface, are seldom much elevated, and are frequently surrounded by a fringe of scales known as the *corona veneris.* The base of the papule is usually quite firmly indurated. The summit is smooth and glistening or capped with a thin firmly adherent scale. Often the papules are so slightly elevated as to be distinguishable from macular lesions only by the sense of touch. Such lesions are known as maculo-papules, or the summit may be converted into a pustule without the base undergoing any change, the lesion then being called a papulo-pustule.

In syphilis scaling papules are frequently met with that are difficult for any but the expert to distinguish from the lesions of psoriasis. The scales here lack the lustrous appearance presented in psoriasis and are not so freely shed. On the contrary, they are frequently so firmly attached to the surface as to require some force on removal, and when the scale is lifted away there are no minute bleeding points found beneath as in the psoriatic lesion. Other lesions can usually be found in the near neighborhood or elsewhere upon the surface of the body that are unmistakably syphilitic.

Papules frequently appear in the palms and on the soles, and in such localities present features somewhat different from any shown in other parts. This is owing to the density of the epidermal coverings in the regions named. Instead of involving the epidermal layers throughout, as is usually the case, they here appear to be buried beneath the epidermis or confined at least to its lower strata. Later they make their way to the surface and become true scaling papules, not at all or only slightly elevated. The epidermis covering the centre of the lesion is first cast off, thus giving to its summit a pitlike depression. The edge of this depression is surrounded by a fringe of torn and dirty looking epithelium. The centres of the palms and soles are the parts usually first to be affected. Later the papules by peripheral extension and coalescence may form scaling patches covering surfaces as large as, or larger than, a silver dollar, or they may remain as distinct and discrete papules, while thickly studding the surface. Extension to the digits may take place. They are not often productive of any sensation.

nently they appear with the first exanthem, and persist during a r the whole of the course of the disease, or they may appear after her symptoms of the malady have vanished, and continue for a ner of years in spite of vigorous and energetic treatment. The on is usually symmetrical, but the right hand is the one most apt everely affected.

ist Papules.—Papules presenting a moist and secreting surface ound upon the skin in situations favoring such development. mth and moisture are necessary conditions, and such factors are d in the axillæ, between the nates, in the perineal region, between scrotum and thigh, within the lips of the vulva, and underneath overhanging breasts of fleshy women. Here the papules begin as e dry form, but are quickly converted into lesions little or not at elevated, and having a circumscribed eroded surface secreting a ky, mucilaginous fluid. Sometimes they are covered by a grayish le looking much like diphtheritic membrane. The lesions when nful and fully developed give forth an almost unbearable odor. is form of moist papule differs in no wise from mucous patches seen thin the mouth cavity. Its structure, development, and complete evolution are the same as the *mucous patch*, and it is frequently called by the same name.

About the mucous outlets of the body a different kind of moist papule is apt to form. This variety is characterized by hyperplasia of e cell elements, with consequent elevation of the resulting lesion. apules of this kind are known as *condylomata* and occur in either a flat or pointed form.

Flat condylomata appear as eminences varying in size from a ten-cent piece to a silver dollar, and having a whitish or grayish white, macerated surface bathed in a tenacious, mucoid fluid or covered with an adherent grayish pellicle. The secretion is extremely offensive in odor and in the highest degree infectious. Often the irritating effects of the secretion beget a similar lesion upon the apposed surface when the condyloma is between the buttocks, so that two lesions of like nature are brought face to face. This form of condylomata may be single or multiple. Frequently the lesions form a complete collarette about the anal or vulvar openings. They are often the seat of intense itching and burning sensations, and productive of the greatest discomfort. Flat condylomata are absolutely diagnostic of syphilis.

Pointed condylomata, or venereal warts, seen so often in syphilitic subjects, differ from the preceding form, not only in their character and appearance, but in the fact that they are not strictly syphilitic lesions. They are produced at any time when the parts are subjected to undue and long continued irritation, such as happens when pathological discharges like those of gonorrhœa and leucorrhœa flow over the vulva, over the perineum, and over the anus, or, in the male, are imprisoned beneath the foreskin. Secretions from certain syphilitic lesions, such as moist papules and flat condylomata, give rise to them as well. Hence it happens that they are found accompanying true lesions of syphilis as an accident only of the process. It is important, therefore, that too much significance should not be attached to this form of condylomata in determining the presence or absence of syphilis.

One or many of these pointed papules may be present. They are filiform or conical in shape, with a broad or narrow base and a tufted apex. When multiple they frequently form masses as large as a good-sized hen's egg. Inspection of such mass always shows it to be made up of a great number of distinct and individual wartlike structures. The lesions may be dry, but are usually covered with moisture. This may be a true secretion on the part of the wart or be sweat arising from the warmth of the part. The lesions are apt to bleed readily and freely upon the slightest irritation or surgical interference. The sulcus coronarius in the male and the inner surface of the labia majora and minora in the female are often the sites of their occurrence.

Absolute cleanliness and the use of disinfecting solutions, such as boric acid, corrosive sublimate, and permanganate of potassium, are the essentials in treatment. If persistent, the lesions may be snipped off with a pair of scissors or removed with a curette, and the base then be touched with a pencil of silver nitrate or a drop of carbolic acid.

Pustules.—Pustules are frequently met with in syphilis. They occur oftenest in the ill fed, unclean, debilitated subjects seen in public practice. Well cared-for patients seldom exhibit them. This fact strongly suggests their being an accident rather than a definite symptom of syphilis, and such belief is gaining ground among syphilographers. Pustules are usually developed from papules. They seldom appear as elementary lesions. The summit of the papule is first converted into a minute vesicle. As this enlarges its contents become turbid, and then pustular. The pustule may be confined to the apex of the papule, occupying only that space first shown in the vesicle, or the entire papule may become involved in the process. Pustules may appear on any part of the body. In the early stages of the disease they are apt to be symmetrical and extensive in their distribution. Later they appear in groups having a circinate arrangement.

The pustules vary in size from a pinhead to a pea. Early in the course of the disease they are small, and more abundantly developed than when occurring at later periods. When first appearing they are discrete, but later may become confluent and give rise to superficial or deep ulcers. The lesions may be clustered in circinate groups or be distributed freely without definite arrangement. Frequently they involve the hair follicle, especially on the face and scalp. A dull ham-red areola is often distinguishable at the base of the pustule or of the papule on which the pustule rests. When ulceration does not follow, the pustules disappear and exfoliation of the epidermal coverings takes place. If the pustules have been large and deep, well marked cicatrices are left as relics of the trouble. Pigmentation frequently occurs, the stain having a dark coppery hue.

Ulcers arise by coalescence of a number of pustules or by enlargement of individual lesions. They are apt to occur late in the disease and in cachectic and anæmic subjects. Only the superficial layers of the epidermis may be involved in the process, or the ulcer may burrow deeply into the skin and subcutaneous tissue. Superficial ulcers are usually small, not often increasing much beyond a ten-cent piece in size. The base is indurated and the ulcer is covered by a light, friable, greenish yellow or dirty looking crust.

In the later stages of syphilis, or early when the disease is pursuing a severe course, large pustules occurring in groups of half a dozen or more may appear at different sites upon the body. These pustules unite and form what is known as the pustulo-ulcerative syphiloderm. This ulcer is deeply seated, frequently painful, and secretes pus in abundance. It is capped by a large dark green or brownish crust, underneath which a well of blood and pus can always be discovered. The pus dries readily, and the resulting crust is more or less firmly adherent to the edge of the ulcer. When the crust is removed and the lesion cleaned of its contents, the ulcer shows a punched-out appearance. The sides are precipitous and the base is uneven and granular. Such ulcers leave a deforming cicatrix unmistakable to the eye of the trained observer.

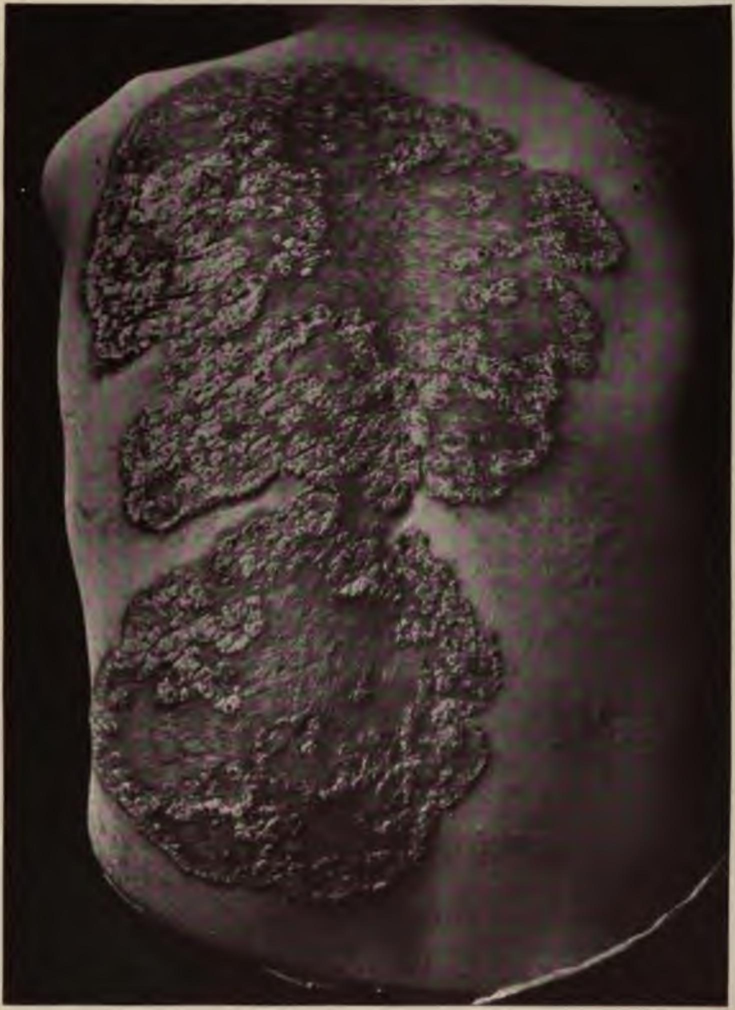
Rupia is a term employed to designate ulcers occurring in syphilis in which the crusts assume a conical or oyster-shell shape. The crust is made up of a number of layers, the one at the bottom covering the greatest extent, and each succeeding layer becoming smaller as the summit is approached. The crusts may reach an inch or more in height and cover an area as large as a silver half dollar. They are produced by successive additions to the crust from beneath, while the ulcer enlarges peripherally. The layer at the top represents the first one formed. The ulcer may be superficial or deep. Rupia occurs only in uncleanly, uncared-for subjects, and generally indicates a severe and persistent type of the disease.

Tubercles.—Tubercles are of frequent occurrence in syphilis. They may appear at any time in the course of the disease after the expiration of the first three months, but are seen more frequently in late rather than in early stages of the malady. They occur oftenest in those cases in which early treatment has been improperly conducted or entirely neglected.

Tubercles differ but little in their characteristics from gummata. They are apt, however, to occur at a somewhat earlier stage and to run a milder and more tractable course. They also appear in greater number and involve the skin less deeply. But in the clinical features that they present it is often a matter of considerable difficulty to distinguish them from the gummy tumors (Plate XI.).

Tubercles may appear upon any part of the body surface, but are found most frequently upon the face and the extremities. The tip of the chin, the alæ of the nose, and the integument covering the knee and elbow joints are favorite sites for their occurrence. They may occur singly, but usually develop in groups of half a dozen or more. They appear as small pea- to bean-sized nodules, set well within the tissues of the skin, and present externally a globoid surface. They are firm to the touch, and in the earlier course of their development are usually painless. In color they vary from a dark red to a coppery hue. Their color varies with any change in the blood supply of the part, such as is apt to ensue after violent exertion. There is then a decided deepening of the previous stain. The circular form of grouping distinctive of syphilitic lesions is here frequently met with. Often extension of the process is by the formation of new rings about or in conjunction with similarly formed groups. In this way figure-of-8 and other odd looking arrangements are formed.

PLATE XI.



Tubercular Syphiloderm, Resolutive and Serpiginous. (Hyde.)

From a photograph of a hospital patient.

Tubercles differ much in the course that they pursue and in the manner in which resolution takes place. Frequently the lesion undergoes degeneration, and absorption of its products takes place without destruction of the overlying integument. This happens frequently upon the face. In such cases there is the formation of a true scar without breaking down and removal of the epidermal layers. The scar is depressed and oftentimes pigmented. The pigment usually disappears in the course of time. Sometimes resolution occurs in this manner in one part of the group while the lesions in another part are still in full process of development.

Degeneration and destruction of the tubercle by ulceration is a frequent method of its removal. Softening of the summit occurs, the roof wall breaks down, and the degenerated products of the lesion are discharged. The ulceration goes on to complete removal of the tubercle, and may extend much more deeply into the tissues. In this latter case the deep extension of the ulcerative process is undoubtedly due to gummatous infiltration of the tissues about and below the tubercle proper. After destruction of the tubercle is complete, repair ensues by the formation of a cicatrix. Frequently, where the process is unrecognized and unchecked, the lesions continue to develop in circles or parts of circles about the sites of existing tubercles, each new crop gradually enlarging the area affected. In this way patches may be formed covering the greater extent of the forearm, the thigh, or one or both buttocks. At the border of the area is the line of advancing tubercles, many of them in a state of ulceration, while within, the process is represented only by the lesion relics of the disease in the form of scar tissue. The process is extremely indolent, and in many cases may continue for a number of years.

Gummata.—Gummata usually occur in the skin late in the course of the disease. In malignant cases or where the progress of the malady is rapid and destructive they may appear within the first six months after infection. They present the appearance of firm nodules deeply set within the skin or subcutaneous tissue. At first they are freely movable over the deeper structures and within the skin itself, but later they become attached to the underlying periosteum, bones, cartilage, or muscles. The skin becomes reddened and inflamed, finally breaking down and permitting the discharge of the gummy mass. Gummata vary in size from a pea to an orange. They are spherical or globoid in shape, or may be flattened and irregular in outline. In their earlier stages they are sensitive in a slight degree only, but later they become extremely tender and painful. They are usually single or but few in number. Rarely they occur in great numbers, as hundreds in one subject. Any part of the body surface may be the seat of gummata, but they are seen with greatest frequency upon the lower limbs and the integument of the forehead and scalp. The effect of gravity acting upon the blood no doubt influences their frequent development upon the limbs.

The tendency of gummata wherever occurring is toward ulceration and destruction of the part. This may occur in the skin with startling rapidity, a few days only sufficing for complete softening and removal of the tissues affected; or the lesion may persist for weeks and months.

with no evidence of change occurring in its substance save that of gradual enlargement. Frequently the gumma extends deeply into the tissues, involving muscle, bone, and cartilage in its destructive course. When this occurs upon the face frightful deformities are likely to result. Thus the cartilages and bones of the nose may be attacked and entirely destroyed, or the lobe of the ear be in part or wholly removed. The severity of the process can only be likened to the ravages made in the same region by malignant disease. The importance of early recognition of the condition is apparent.

Ulcers resulting from the destruction of gummata are apt to be sluggish and indolent in their deportment. Their size is determined by the lesion from which they arise. They are circular, oval, or irregular in outline. The edges may be thickened or undermined, the sides precipitous, and the floor uneven, foul, and dirty with brown or greenish colored pus. In cachectic and poorly nourished patients such ulcers may become the seat of gangrene. When the necrotic mass is entirely eliminated the ulcerative process ends and repair begins. Healthy granulations cover the floor and sides of the ulcer, the thickened edge is smoothed out, and the process is completed by the formation of a cicatrix. This cicatrix is circular in outline, smooth, white in the centre and pigmented at the border. The scar is deep and firm, usually being attached to the parts beneath. Its recognition is frequently of great value in establishing a diagnosis of preceding syphilis.

At times a diffuse gummatous infiltration of the skin or subcutaneous tissue takes place. This is apt to occur over the back or upon the lower extremities, as the parts of the leg between the knee and ankle. The skin becomes reddened, swollen, tumefied, and sodden. Nodules appear at various points, break down quickly, and discharge their typical gummy exudate. The process if unrecognized may go on for long periods of time, resulting in great thickening of the integument and the production of abundant scar tissue, or the entire gummatous area may break down, forming a single gigantic ulcer. Upon the abdomen gummatous infiltration is apt to result in a serpiginous ulcer. Gummata are, however, rare in this location. In the genital region such infiltration results in contraction and deformity of the penile organ or in narrowing of the entrance to the vagina.

Affections of the Hair due to Syphilis.—The hair is frequently affected in the course of syphilis. The nutrition of the filaments may be impaired in so slight a degree as to give rise only to a certain amount of dryness and lack of lustre, or the process may be so severe as to bring about an extreme and deforming alopecia. These syphilitic alopecias are important from a diagnostic standpoint because of the help they furnish in arriving at exact conclusions regarding the existence of the disease. They appear as the result of one of two processes: either the hair falls as the result of defective nutrition, with no structural change occurring in the part from which it arises, or there is a preceding organic change in such part. The alopecia in the first form may be said to be due to a primary process, while in the other it is secondary.

In the primary form the hair may come out slowly or very abruptly. There may be a gradual thinning of the hair of the scalp and of other parts of the body, a few filaments only coming away each day, until the complete loss becomes decidedly apparent, or the process may be characterized by the development of numerous bald patches no larger in size than a ten-cent piece. When these patches occur upon the scalp they affect the back and sides of the head more than other parts. In these regions the bald areas are set so thickly as to almost occupy the entire surface. They give to the hair of the head a characteristic "ragged" appearance not seen in any other form of baldness. The patches are irregular in shape; the surface is scaly and often set with a few dead stumps of hairs, as in ringworm, and the color is a dead grayish white. The eyebrows, beard, hairs of the pubic region and of the axillæ may share in the process. Usually the hair in these parts does not fall independently of that on the head. The loss is apt to be asymmetrical, and, when this occurs in the case of the eyebrows or beard, results in peculiar disfigurement. The eyelashes are not often affected. The hairs remaining are loosened and can be readily removed from their pouches. This form of syphilitic alopecia is by far the most common and occurs most frequently in the early stages of the disease, accompanying or shortly following the appearance of the exanthemata. While productive of much mental discomfort, it is not a serious misfortune, as the hair is always replaced under simple and appropriate treatment.

The secondary form of syphilitic alopecia results from previous changes in the integument due to the presence of syphilodermata. Such syphilodermata may be in the form of macules, papules, pustules, tubercles, ulcers, or gummatous infiltration. The loss of hair occurs as the result of partial or complete destruction of the hair follicle. The process belongs to a late period of the disease, but in severe forms of syphilis it may occur early. The alopecia is permanent if the hair follicles be entirely destroyed. If destruction is not complete, there may be a partial and stunted growth. The scalp is the part usually affected and in limited areas only.

Syphilis of the Nails.—Syphilis may attack the nails at any time in the course of the disease. The affection may begin in the nail itself, and its manifestations throughout be confined to the nail substance, or it may begin in the soft parts and later extend to the nail tissue. The first form is called *syphilitic onychia*, and the second *syphilitic paronychia*.

Syphilitic Onychia.—Changes in the nail substance are characterized by loss of lustre, formation of puncta, striæ, brittleness, and deformity. These changes are due to disturbances in nutrition, and are common in the earlier periods of the disease. Careful examination of the nails shortly after the outbreak of constitutional manifestations will usually show perceptible changes in their structure and appearance. The nail often appears dead, and along its border a pale white line shows where nutritional changes are taking place. With the atrophic condition there may be an accompanying hypertrophy of parts of the nail, leading to the formation of longitudinal lines and ridges much elevated above the surface; or the nail may be greatly thickened throughout, while over the surface characteristic striæ and puncta, due to the accompanying atrophic condition, can be detected. These changes may lead to complete or partial removal of the nail. One or all of the nails may suffer. The nails of the fingers and those of the great toes are most frequently attacked, *Syphilitic Paronychia.*—This form begins as an inflammatory con- on at the base or sides of the nail. It may be superficial, only the dermal structures being involved, or it may extend so deeply as to olve the distal phalanges of the digits. The parts are greatly thickened, and at times there is the production of a mass of new tissue hav- s decidedly verrucous appearance. Fissures and excoriations form the part may become exceedingly tender. The nail is affected as cribed under Syphilitic Onychia. It is usually first elevated at one ne, and then gradually pushed off. The process may occur at any time during the first two years after infection. The nails of the fingers suffer more frequently than do those of the toes, owing probably to their exposed position and their greater liability to injury. The process is apt to pursue an indolent course, but the final results of energetic treatment are good, and in the end the integrity of the nail is restored.

Syphilis of the Mouth and Tongue.—Syphilitic affections of the mouth and tongue are of frequent occurrence. The nature of lesions appearing in the mouth and tongue demands early recognition owing to the extremely infectious nature of the secretions they furnish and the ready means by which the virus can be transmitted from these parts to sound individuals. Any of the various lesions displayed upon the skin during the entire course of the disease may appear upon the mucous membranes of the mouth and throat. They are modified somewhat by varying conditions of heat, moisture, and friction to which they are here subjected. Frequently they pursue an obstinate and intractable course, and at times occasion a marked degree of distress. Often the mouth cavity shows the only evidence that the individual is affected with or is still suffering from syphilis, and the lesion relics in the form of cavities and scars remaining after the disease displays no further active manifestations furnish valuable evidence as to its previous existence.

The initial sclerosis is found upon the lips or within the mouth cavity with greater frequency than upon any other portion of the body, excepting the genital region. Its occurrence here is not in the innocent only, but is frequently the result of vile and disgusting practices. Chancres appear upon the lips having the typical features elsewhere described. They are usually single, but may be double, one appearing upon either lip in direct apposition to each other. The lower lip and the median line furnish the site of their most frequent occurrence. Fissures, cold sores, and cigarette-burns upon the border of the lip often furnish the solutions of continuity through which the poison enters. The pre-existence of such lesions modifies in a measure the features presented by the developing chancre.

Chancre of the tongue occurs either at the tip or upon its anterior half. The lesion usually appears as an erosion or as a nodule superficially seated and indolent in its course. Induration is marked if the tip of the tongue be its seat, but if placed upon the dorsum or sides it may be slight and easily overlooked. The submaxillary and subhyoid glands enlarge and the degree of induration is often very great. It is important that the chancre should be distinguished from tuberculosis and cancer, both of which are apt to occur in these situations. In tuberculosis the onset of the malady is slow, the lesion is very painful, and the accompanying glandular enlargement is slight. Discovery of tubercle bacilli in the lesion or its secretions definitely determines the diagnosis. Cancer is more difficult to distinguish. It begins as a nodule and its accompanying adenopathy is great. Its development is slow, and it occurs usually in individuals well past middle life, while syphilis is apt to occur before that period is reached. Cancer is seen in tobacco smokers, the site of the lesion being that part of the tongue coming in contact with the tip of the cigar or pipe. Cancer of the lip occurs most frequently near the angle of the mouth, while chancre, as has been noted, appears near the median line. A short delay, with or without the exhibition of mercurials, will involve no peril and will enable the physician to reach a satisfactory and conclusive diagnosis.

The tonsil is the occasional seat of chancre. The lesion here presents no constant and characteristic features because of the peculiar formation of the tonsillar tissue, this differing in each individual. There is usually much distress in swallowing, and the pain may often be continuous and severe. The neighboring ganglia in the neck become very much enlarged and densely indurated. Induration of the tonsil sometimes occurs, but is not constant. Considerable difficulty is sometimes experienced in distinguishing between the malady and a chronic tonsillitis. In tonsillitis there is usually a history of previous attacks, and an accompanying coryza with a greater or less degree of temperature. There is but slight enlargement of the glands in the neck, and these are tender and painful to the touch.

Chancres may appear upon the gums, cheeks, or soft palate, but are exceedingly rare in these situations. Chancres of the lips and mouth cavity are liable to persist until the development of constitutional syphilis, and then to be converted into moist papules or mucous patches of the parts.

Constitutional syphilis may be represented in the mouth by macules, papules, pustules, tubercles, ulcers, and gummata. Hyperæmia of the pharynx, fauces, and soft palate occurs with or shortly after the appearance of the erythematous syphiloderm. The hyperæmia is bright or dark red in color, usually extensive, and diffuse or bordered by well defined outlines. It may also appear in spots varying in size from a pin-head to a ten-cent piece. These spots may be few in number or scattered thickly over the walls of the pharynx, cheeks, and roof of the mouth. The throat is dry, and is the seat of somewhat painful and uncomfortable sensations. Deglutition is accompanied by considerable distress. The hyperæmic condition usually subsides quickly under treatment. Mucous patches or ulcerative lesions of severe type may follow. The delicate, moist epithelium may be removed by maceration, with the production of raw-looking ham-red patches varying in size from a pin-head to a ten-cent piece. The ulcers are oval or linear in shape and have a punched-out appearance, with a grayish pus-secreting floor.

Papules are represented in the mouth by the mucous patch. That there is no distinction to be made between the two is evidenced by the readiness with which the papule occurring on the skin when subjected to heat and moisture is made to take on characteristics that render it in no wise distinguishable from the mucous patch in the mouth. These mucous patches may be the result of transformation of a chancre occurring in the part, as has been noted, or they may develop independently d primarily. They then begin as reddened, circumscribed macules in mucous membrane. Elevation, due to multiplication of the cells in the substance of the lesion, soon follows. Removal of the epithelial vering by maceration and friction follows, and the lesion takes on a yish white appearance, as if the part had been touched by a pencil silver nitrate. Mucous patches occur singly or in groups. Often they come in successive crops. Coalescence may ensue, with the formation of an irregular patch varying much in size. Neglected cases frequently show the entire roof wall of the mouth or the inner surface of the cheek covered by a lesion of this nature. Patches occurring upon the cheek or tongue are apt to beget like lesions upon the surfaces with which they come in contact. Favorite sites for their appearance are just within the angles of the mouth and underneath the tongue. When occurring upon the surface of the tongue they frequently have a glistening, shiny look, and may appear depressed instead of being elevated. This is due to the elevation of the surrounding papillæ. The shining appearance is produced by the removal of the epithelium and the exposure of the rete layer beneath. Mucous patches are often painful, and when seated upon the walls of the pharynx occasion considerable distress in swallowing.

Hypertrophy of the patch may occur as the result of its infiltration with small round cells. When such patch is situated on the cheek near the labial angle it often becomes deeply fissured, owing to the movement of the parts in mastication, and it then becomes exceedingly painful. It may even pass beyond the angle of the mouth and extend for some distance upon the surface of the cheek. Hypertrophy of mucous patches upon the surface of the tongue gives rise to lesions having very much the appearance of venereal warts. This form has given rise to its designation as the "toad's-back" tongue. Lesions of this class belong to the type of moist papules seen so frequently in syphilis about the anus and vulva.

Ulcerative lesions resulting from the papules are not rare, and are due to irritation of the parts and their infection with pus cocci. Such ulcers are apt to be deep and destructive in their course and to be productive of considerable pain.

Syphilitic lesions occurring in the mouth are often the result of undue irritation of the parts. The use of tobacco, either by smoking or chewing, the ingestion of hot or very cold fluids, indulgence in highly spiced articles of food, and the presence of decayed or roughened teeth are frequent and prolific sources of mischief.

Pustules occur in the mouth but rarely. They are produced by infection of papular lesions with pus-producing bacteria. When pustules appear in the mouth, lesions of the same character can usually be found upon the integument.

Fissures may be formed, as described, in connection with moist papules or independently. The commissures of the lips and the surface of the tongue are favorite sites for their appearance. At the angle of the lips the condition is aggravated by the motion of the parts, and extension of the process to the cutaneous surface may take place as in the case of moist papules. Fissures are slow in healing and may leave deforming cicatrices. Upon the surface of the tongue they usually present themselves as long linear cracks extending deeply into its substance. Often they appear as if the tissues had been deftly divided by a sharp knife. Their walls are then in close contact, and their separation is needed to reveal the extent of the fissure. Fissures usually follow mucous patches or areas of small-celled infiltration.

Tubercles occurring upon the tongue and mucous membrane of the mouth resemble enlarged or hyperplastic moist papules. They are rounded or flattened nodules involving the tissues somewhat deeply, and occurring at points where there is but little pressure, as on the under surface of the tongue.

Gummata do not develop in the mouth until a late stage of the disease has been reached. They may occur in any part, but most frequently attack the tongue. They begin in either the deep or superficial tissues, and are apt to run a much more rapid course than when occurring elsewhere upon the body. The superficial variety is first noted as a small, round, reddened nodule appearing in the mucous membrane. The nodule is slightly elevated and is moderately firm to the touch. The lesion may increase in size slowly, but its most frequent course is to enlarge with startling rapidity. The centre becomes necrotic, caseous degeneration follows, and the roof wall, which at first is tense, is broken down and a gaping ulcer results. There may be but one or there may be several of these lesions scattered over the tongue, the hard palate, and the cheeks. The gummata are seldom painful, and often are not discovered until softening and ulceration have occurred.

Gummata originating in the deeper structures, such as the muscular tissues of the tongue and the bones of the hard palate, are apt to be much more formidable and severe in the course they pursue. The neoplasm usually occurs singly. Its onset is insidious and without pain. It is a circumscribed, indurated, firm tumor, varying in size from a hazelnut to an olive. Degeneration and ulceration occur at times with great rapidity. Perforation of the palate may take place within a week from the first appearance of the nodule. If not promptly checked, the process may go on to more or less complete destruction of the roof wall. Ulcers in which a marble may be hidden destroy with the same rapidity the tissues of the cheek and tongue. The ulcers are round, oval, linear, or irregular in shape. Their edges are elevated and roughened or sometimes undermined. Even with the most marked ulceration the pain is not often severe. The prognosis is good. Repair of the soft tissues occurs with the production of cicatrices that are markedly deforming. Destruction of the hard palate can be remedied by the use of an obturator. Treatment must be energetic and chiefly by the use of the iodides, pushed in increasing drop doses of the saturated solution until the ulcer yields. Locally, antiseptic washes and stimulating applications of carbolic acid, iodine, or silver nitrate are of decided value. Tonics such as iron, strychnine, and quinine are usually needed.

Syphilis of the Digestive Tract.—Syphilis seldom attacks the œsophagus. Gummatous infiltration of its walls, resulting in cicatricial stenosis and narrowing of the lumen, has been described. Little is known definitely regarding syphilitic affections of the stomach. Gummata have been discovered in post-mortem examination of syphilitic subjects in whom no appreciable gastric symptoms were present during life. Gummatous infiltration of limited or extended areas of the mucous and submucous tissues may result in considerable fibrous thickening of the walls of the organ. In the intestinal tract the rectum suffers with greatest frequency and needs separate description. Elsewhere the walls of the intestine may become the seat of gummata. These are superficial and seldom give rise to serious symptoms.

Syphilis of the Heart and Bloodvessels.—Syphilis appears to find in the vascular system conditions favoring its first expression. In the chancre, before marked invasion of the body by the syphilitic virus has taken place, constant and characteristic changes are noted in the vessels entering and leaving the part, and throughout the course of the disease the bloodvessels are apt to suffer in a marked degree. This is doubtless due to the abundant development of connective tissue entering into the formation of the arteries and veins.

The Heart.—The heart suffers less frequently than do the vessels, but when affected the intensity of the trouble is greater and more serious mischief is apt to result. Not infrequently a fatal termination ensues. Manifestations of syphilis in the heart usually appear late in the disease. When attacked the heart may become the seat of gummata or a specific fibrous myocarditis may develop.

Gummata may occur in any part of the heart, but appear most frequently in the endocardium, along the edges of the valves, and in the interventricular septum. The neoplasms vary in size from a pinhead to a hazelnut, and appear as circumscribed, spherical, non-vascular, yellowish or whitish bodies set somewhat deeply in the tissues affected. They show on section a necrotic, cheesy centre surrounded by a connective tissue capsule. From this capsule strands of fibrous tissue can be seen radiating into the surrounding parts. No trace of muscular elements remains at the site of the nodule. They appear to have undergone fatty degeneration with complete absorption. Small gummata have been found in the chordæ tendineæ. When this occurs, shortening, thickening, and weakening of these structures take place. Death produced by their rupture has been known to follow. In stillborn infants affected with hereditary syphilis the heart has been found thickly studded with minute gummata.

Fibrous myocarditis of the heart due to syphilis occurs as the result of an arterio-sclerosis or obliterating endarteritis of the coronary arteries. The part of the heart supplied with blood by the branches of the particular artery affected becomes impoverished, undergoes degeneration, and its structures are replaced by fibrous tissue. Any part of the heart may be affected. Frequent sites of its occurrence are the papillary muscles and the septum. These parts are thickened, become dense and firm, and are found on section to be composed almost entirely of fibrous connective tissue with only a meagre vascular supply. Occasionally spindle cells are found mingled with the fibrous elements. Gummata frequently exist in intimate association with this form of affection. The endocardium in some cases undergoes a like fibrous change. It is then greatly thickened, becomes gray or grayish-white in color, and takes on somewhat the consistency of cartilage. The rigidity produced often interferes greatly with the action of the heart.

Aneurysm of the heart walls bounding the ventricles may occur. This happens as the result of softening and excavation in a gumma opening into the ventricular cavity, or it is due to the dilatation of an area of fibrous myocarditis. The walls of such aneurysms are composed of dense fibrous tissue, and their cavities are frequently filled with thrombi.

The symptoms produced by syphilitic disease of the heart are not distinctive. The history of each case as regards skin lesions and other characteristic symptoms must usually be relied upon to establish the diagnosis. By some it is thought that the dyspnœa occurring in diseases of the heart is apt, when the trouble is due to syphilis, to come on more frequently at night when the patient is resting quietly in bed. This fact, however, is not well established, and too much reliance should not be placed upon its diagnostic importance. Many persons suffering with syphilis with marked involvement of the heart go through life without manifesting any signs of trouble in the organ, the condition only being disclosed at the autopsy. With obliterating endarteritis of the coronary arteries and its resulting heart lesions death may ensue suddenly and without marked prodromal symptoms.

The Bloodvessels.—Syphilis affects the bloodvessels both early and late in the course of the disease. The greater part of its energy is expended upon the arteries, while the veins very largely escape. Little is known regarding the effects of the disease on the capillaries. Fatty degeneration and gummatous changes in their walls have been observed.

The most frequent lesions met with in the walls of the arteries are gummata, aneurysm, arterio-sclerosis, and obliterating endarteritis.

Obliterating Endarteritis.—This is by far the most frequent and serious trouble occurring in the arteries that is due to syphilis. The smaller arteries are principally affected. There is partial or complete closure of the lumen of the vessel due to proliferation of the endothelial elements in the intima. The specific virus of the disease or the product of such virus circulating in the blood excites the proliferation by means of its irritative action. Thickening of the intima takes place, layer after layer of the endothelial cells forming one within the other until the vessel is nearly or entirely closed. The adventitia is attacked, and gradually all the coats of the vessel become affected. A true inflammation may be excited, with subsequent production of granulation tissue. This latter is converted into fibrous connective tissue having a marked tendency to contract. If the lumen of the vessel is still partly patent, the contractility of this newly formed tissue is usually sufficient to close it. The nutrient vessels are made to share in the process and are completely obliterated. The process is usually confined to limited and localized areas. The arteries at the base of the brain and the coronary arteries suffer most frequently. Arteries in any part of the body, however, may be affected.

Gummata.—Gummatous changes occur in the larger arteries. They are localized or diffuse. The adventitia suffers more often in the circumscribed form than do the other coats. The lumen of the vessel is partly closed by pressure of the mass inward. The narrowing is still further accomplished by thickening of the intima. Thrombi frequently form at the narrowed point. The gumma undergoes its peculiar changes, softens, discharges its contents into the circulating blood, and then becomes the seat of an aneurysm. In the diffuse form the gummatous infiltration occurs between certain of the vessel's coats, such as the intima and adventitia. The entire circumference of the vessel wall may be involved or only a part be affected, while the process may extend along the artery for some distance. Fatty or cheesy degeneration of the gummy infiltrate takes place, and later calcification, leading to the production of atheroma. The carotids and arteries of the brain appear to suffer most frequently. The weakened walls of vessels affected in the brain are liable to rupture suddenly when subjected to strain and give rise to apoplectic seizures.

Arterio-sclerosis.—Syphilis is one of the many causes capable of producing arterio-sclerosis of the bloodvessels. This condition when due to syphilis is seen most frequently in robust individuals between thirty and fifty years of age who have suffered from the disease in early life. The affection is apt to be generalized. The lumen of the vessels is enlarged, instead of being narrowed as in endarteritis. The intima is thickened and often becomes the site of atheromatous change. The walls throughout are hardened and inelastic. To the touch they feel like whipcords placed beneath the skin. The condition is in no wise distinguishable from the same disease when it is caused by alcoholic or lead poisoning or gout, nor does it appear more amenable to treatment. Iodide of potassium in full doses is indicated and may be tried in interrupted courses, pushing it each time to the patient's limit of tolerance. A well regulated, quiet life must be insisted upon.

Syphilis of the Genito-urinary Organs.—In men the penis is frequently the seat of the initial sclerosis. This has been described (page 854). Œdema and diffuse swelling of the organ are complications liable to occur in connection with chancre, especially if the lesions be large and subject in any manner to irritation. Phimosis and paraphimosis are produced as complications. The organ then is swollen, hot, and tender. The lymphatics become inflamed and painful, and seem to the touch like whipcords running along the dorsum of the penis and encircling its root. These conditions, while productive of some discomfort and much alarm on the part of the patient, seldom occasion serious mischief. Rest, elevation of the organ, frequent immersion in warm boric acid solution, and the administration of a laxative internally usually suffice for their removal.

The glans penis, owing to interference with the return circulation by the chancre, sometimes assumes a bluish color, suggestive of gangrene. This is apt to occur with large, deeply indurated chancres situated in the sulcus coronarius. The discoloration vanishes with resolution of the chancre. Balanitis and posthitis may result from irritating discharges from the primary sore.

Consecutive lesions occur in the varying forms seen elsewhere upon the surface of the body. Scaling papules may be found at times upon the glans penis when no other lesions indicative of syphilis can be discovered. A slight catarrhal discharge from the urethra is sometimes noted as occurring in early syphilis. This is probably due to the presence of mucous patches within the walls of the passage. Gummata appearing as firm, spherical nodules occur within the corpora cavernosa. They develop slowly and without pain, the patient first noting that the penis is "crooked" when erect, and later discovering a "lump" deep within the tissues of the organ. The tendency of such neoplasms is toward degeneration, with absorption of the products and the subsequent development of circumscribed areas of fibrous connective tissue. Permanent deformity of the organ then results. Gummata are not apt to occur in the corpus spongiosum. When doing so they give rise to exceedingly rebellious strictures of the urethra.

A peculiar condition resembling a circular band placed about the penis results occasionally from a fibrous development taking place within the cavernous bodies. This band may encircle the penis completely or only in part, and usually interferes greatly with perfect erection of the organ.

Syphilitic affections of the testicles and their appendages are common, but, owing to the slight distress occasioned, are often overlooked. It should be the invariable rule of the practitioner to examine these organs at the time of the patient's first presentation when the body is searched for specific lesions, and throughout the course of the disease the testicles should be watched with care. Trouble occurring here may show itself early or late. The epididymis usually betrays some slight degree of irritation at the time of the first eruption. It becomes somewhat swollen and is painful to the touch. Later in the course of the disease a circumscribed area may become the seat of inflammation. This is a true specific epididymitis, and is to be distinguished from that due to gonorrhœa by its slow, insidious, painless onset, and by the fact that the globus major instead of the globus minor is the part most often affected. One or both organs may be attacked. Circumscribed gummata or diffuse areas of gummatous infiltration occur late in the disease. They are painless and slow in growth. The gummatous infiltration may involve the entire epididymis or be confined to a portion of the organ only. The discovery of a lump in his testicle is often the first indication given the patient of existing trouble. Extension of the process to the testicle proper and to the cord often takes place. When discovered early treatment is usually successful in removing the deposit and saving the organ. If neglected, irreparable damage may be done and a useless organ may result.

Trouble in the testicle usually begins late in the disease, and is due to the formation of gummata. These may appear first in the substance of the testicle, or they may begin in the tunica vaginalis investing the organ, and from this extend to the deeper structures. In the tunic they can be felt as small, round, firm, freely movable nodules. If deep in the testicle, they cannot be detected by touch until they have enlarged to a considerable extent. There is no pain. They may be single or multiple. The testicle may be invaded throughout its entire substance by the gummatous deposit or the process be limited to a portion only of the organ. The gummata enlarge slowly. Their substance is dense, often as hard as ivory. The testicle increases in size, sometimes becoming as large as a child's head. Its weight drags upon the cord, producing uncomfortable sensations in the groin and abdomen. Aside fro this there is no pain. Pressure, unless excessive, elicits little sponse. The surface is smooth. In this it differs from tuberculosis, which the organ is uneven and rough. Occasionally there is effusion fluid into the tunica vaginalis with the formation of hydrocele. One both testicles may be affected. The course of the malady is exceed-gly slow, years often being occupied in the process. The trouble ds in absorption of the gummy exudate and the development of brous tissue, leaving a shrunken, withered organ, or softening of the umma may result in complete destruction of the testicle. This, how-ver, is unusual. Fungous growths sometimes arise. During the prog-ss of the affection there is oftentimes no marked change in the sexual ppetite.

Syphilitic orchitis responds readily to specific treatment begun early n the attack and pushed with sufficient vigor. The iodides are indicated n full doses. Locally, inunctions of the oleate of mercury in 5 per cent. strength are of value. The tendency of the disease is to destroy the seminiferous tubules, and when such destruction has taken place repair cannot ensue.

In women chancres occur as frequently upon the genitals as they do in men, but, owing to their being hidden from sight, are not as readily recognized. The os uteri and vulvar portal are favorite sites. Chancres are seldom seen upon the vaginal walls. They may occur in the urethra. The early lesions of systemic syphilis may develop upon the vulva and within the vaginal canal, most frequently as condylomata or mucous patches. Condylomata present the features described elsewhere (page 862). Mucous patches occurring upon the vaginal walls differ but little from those appearing in the mouth cavity. These patches give rise to but little distress unless irritated by leucorrhœal discharges. In such cases the lesions are greatly aggravated and frequently very painful. Mucous patches of the vagina and os uteri, whether occurring early or late in the course of the disease, are undoubtedly the most fruitful source of infection.

The posterior wall of the vagina may be involved in the syphilitic affections occurring in the rectum. The remainder of the tract is not often the site of gummata. Little is known regarding early syphilitic affections of the uterus and ovaries. In both, gummata may develop in later stages. In the ovary the changes taking place resemble those occurring in the testicle. The gummatous deposit may be diffuse or circumscribed and lead to wasting and shrinkage of the organ.

The *bladder* is rarely attacked by syphilis. It is believed to be affected slightly in the early stages of the disease, but little is known regarding the condition. At the most, it is probably but a transient hyperæmia. Gummata, papillomata, and hypertrophic growths due to syphilis occur in later stages. Fistulous tracts may be formed by extension of ulcers occurring in neighboring organs.

The *kidney* may be affected at any time in the course of the disease after the development of systemic syphilis. Early manifestations of trouble differ very much from those occurring at later periods. They are sudden in their onset, not often being announced by any prodromal symptoms. Œdema occurring in and beneath the lower eyelids is usually the first evidence furnished showing that the kidney is affected. This is more noticeable in the morning after the patient rises from rest than later in the course of the day. The œdematous condition later appears in the extremities and in other parts of the body.

Examination of the urine shows albumin in small or large quantities, granular casts, blood, pus, and kidney epithelium. The amount passed in twenty-four hours is somewhat lessened or even greatly decreased. The specific gravity is high and the color dark. The urine is turbid when first passed. Calls to urinate are frequent, though the amount passed each time is small.

Other symptoms referable to the condition of the kidneys are evidenced in headache, vomiting, malaise, inappetence, digestive disturbances, and disordered vision.

Post-mortem examination of the kidney at this time shows well marked organic changes in the renal substance. The organ is much enlarged, and appears gray or grayish white on section. The cortical portion is thickened, the epithelium in the convoluted tubules swollen, and the tubes in places filled with broken-down tissue and catarrhal products. The organ is in the condition known as large white kidney.

Early syphilitic affections of the kidney usually respond promptly to proper mercurial treatment. At times, however, the administration of mercury may aggravate and intensify the process. In such cases resort must be had to the iodides, the iodide of potassium having the preference. It is well always to examine the urine at frequent intervals in a patient under treatment for syphilis, in order to anticipate trouble occurring in the kidney. It is particularly desirable to do this after an albuminous attack, as recurrences are frequent. Rest and a milk diet will help in restoring the kidneys to a sound condition.

Late changes in the kidneys are more severe and disastrous in their results than are the earlier lesions. The process here is usually complex in character and referable to several distinct and separate conditions. Principal among these are the formation of gummata, amyloid degeneration, and inflammation of the interstitial connective tissue. These processes operate in conjunction in various degrees, though rarely one may exist singly. Usually both kidneys are affected. The symptoms depend upon which one of the above conditions is most fully developed. If interstitial inflammation be the chief lesion, the urine will be increased greatly in quantity, its specific gravity will be low, and the quantity of albumin will be small. If amyloid degeneration exists alone or exceeds the other complications in its gravity, the urine will be but slightly increased in quantity, albumin will be abundant, hyaline and waxy casts plentiful, and free fat globules with degenerated cells will be present in the flocculent precipitate. Purely gummatous changes, unless so extensive as to interfere greatly with the function of the kidney, are said not to be productive of definite symptoms. Gummata are often found post-mortem in the kidneys in subjects in whom during life no definite renal symptoms were exhibited.

In chronic interstitial nephritis due to syphilis the process is usually localized. The areas of implication are contracted, giving to the surface of the organ when seen in post-mortem examination an irregular, uneven appearance. Gummata are often found in or near the affected areas. They may be few in number or numerous, and vary in size from a pinhead to that of a hazelnut.

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confined to the base of the lung, rarely approaching the apex. In this respect it differs markedly from tuberculosis.

In stillborn infants the lungs are frequently affected with what has been described as *white pneumonia.* The lung is dense and hard, the alveolar walls are thickened and infiltrated, and the air cells are choked with epithelial débris.

The symptoms occurring in syphilis of the lung are not distinctive. The affection comes on slowly and without fever or pain. The respiratory act grows feeble. There may be dulness over limited areas at the base of the lung. Cough is usually mild and accompanied by slight expectoration. At times, however, it may be severe. Bleeding from the lungs sometimes takes place. Asthmatic attacks occur. And finally, as the disease becomes thoroughly established, it exhibits many of the signs and symptoms displayed in tuberculosis and may end fatally.

Evidences of syphilis in other organs of the body and a definite history of a previous attack are essential elements in diagnosis. Gradual development without fever, pain, or distress in the lungs points to syphilis. The early involvement of the base instead of the apex of the lung helps to distinguish it from tuberculosis. The discovery of tubercle bacilli definitely determines the existence of the latter disease. Marked dyspnœa occurring at night is believed to be a typical feature of the syphilitic affection.

Syphilis of the Liver.—Syphilis manifests itself in the liver either in the production of gummata or in the development of fibrous connective tissue. Early in the course of the disease icterus is apt to occur. This is due only to functional disturbances occurring in the liver. The process is seldom severe and always transient. Gummata are usually a late development. They occur in small or large numbers and in any part of the organ. In their earlier stages they are small, firm nodules composed largely of connective tissue. Spindle and small round cells are scattered throughout their substance. The connective tissue sends radiate processes into the surrounding parenchyma. When the lesion is situated near the capsule the surface of the organ is apt to show a depression due to contraction occurring in the connective tissue elements of the underlying gumma. Gummata here undergo various forms of degeneration. Softening and ulceration occur, but are infrequent. Caseous degeneration with absorption of the product and the development of fibrous connective tissue are more usual. Calcification may occur. Contraction of the areas affected often takes place in such way as to produce appearances resembling new lobes. At first the liver is enlarged, oftentimes so as to be noticeable on palpation and percussion. Later, owing to contraction of the resolving gummata, it becomes much reduced in size. The gummatous development is apt to be particularly free in the neighborhood of the suspensory ligament.

Development of fibroid tissue occurs in the liver without accompanying gummatous change. In such case the fibroid tissue appears to arise in the capsule of the organ and to penetrate the liver in broad or narrow bands. The septa thus formed are again intersected by li bands arising in the larger bundles. In this way the organ is divi into a number of separate and distinct lobules. The process is cl and rebellious to treatment. Atrophy of the portions affected usually results.

Syphilis of the Anus and Rectum.—Syphilitic affections of the anus and rectum are liable to occur at any time in the course of the disease. Chancres are frequently found here, infection in women being due to misplacement of the penile organ, and in men occurring as the result of disgusting practices. If the chancre occur within the sphincter ani, it is rarely discovered. On the anal border or upon the perianal surfaces it presents itself as a firm flat or spherical lesion, somewhat resembling a small hemorrhoid. It may also appear as an eroded surface or as an anal fissure. The lesion is usually painless, but may be the seat of considerable distress when straining at stool.

The early consecutive lesions occurring about the anus are either in the form of macules or papules. They appear usually in conjunction with the first macular exanthem. Syphilitic lesions occurring in this region are often intensely pruritic. Papules about the anus, in consequence of the heat and moisture incident to the part, are liable to be converted into mucous patches and condylomata. The secretion furnished by such lesions is extremely contagious in character, and it possesses a most offensive odor.

Late affections of syphilis occurring in the rectum are more commonly met with in women than in men. They consist of gummatous infiltration of the parts and the free development of fibrous connective tissue.

Gummata may form at any point within the rectum. They may be single or multiple and localized or extensive in distribution. Diffuse gummatous infiltration may envelop the entire surface of the gut in a broad band or extend along one of its sides for a considerable distance. When small, gummata are apt to be numerous. Their point of origin is in the mucous or submucous tissues. In their earlier development they feel to the tip of the finger like smooth, round, firm nodules set somewhat deeply within the rectal tissues. Later they become elevated, less firm, and often develop into papilliform bodies. Ulceration occasionally happens.

Gummata of the rectum are not often painful. The first symptoms of trouble are usually a prolonged and constant or intermittent diarrhœa. This is followed by obstinate constipation, with uneasy and painful sensations occurring in the rectum when at stool. When the gummy infiltration encircles the gut, stricture is almost sure to result. This is accomplished by absorption of the gummatous material and the production of fibrous connective tissue. A chronic proctitis usually accompanies such stricture, and the discharges from the bowel are liquid in character. Steady and progressive contraction of such strictures is apt to continue until the lumen of the bowel is so greatly narrowed as to interfere in a dangerous degree with the discharge of the intestinal contents. Examination with the finger-tip shows the lumen narrowed in various degrees, a roughened, corrugated, dense mass of contractile tissue encircling the gut, a pouch-like expansion above it, and tongue-like projections of rectal tissue beneath. Strictures arising in this manner have been called by the French ano-rectal syphilomas.

Taylor has described a form of stricture occurring in the rectum, due to syphilis, characterized by the formation of dense fibrous tissue without preceding inflammatory conditions or exudative products taking place in the parts. It occurs in young and old syphilitic women long after symptoms of the disease have ceased.

Syphilis of the Bones.—Syphilis is liable to affect the bones or their periosteal coverings at any period early or late in the course of the disease. As a rule, the attack is late, several years elapsing between the appearance of the chancre and the time when definite lesions of the bones first show themselves.

The earliest effects of syphilis manifested in the osseous system are what are known as osteocopic pains. These pains occur at or about the time of the first exanthem or even before it. They are not always present: in some cases they are light and transient, while in others they are extremely severe and produce the most intense suffering. The pains are grinding, boring, or splitting in character, and are usually referred to the joints with deep extension into the bones forming such parts. The knee, elbow, and shoulder joints are most frequently affected. The pains are not stationary, but shift from one part to another with considerable rapidity. They are worse at night, often occurring at a given hour and making rest for the remainder of the night impossible. During the day complete freedom from pain is often experienced. Patients, if they be aware that mercury is being given them, often attribute these pains to its use. This idea is entirely erroneous, and there is no indication for cessation of the drug if the pains come on after its use has begun. Its dosage should rather be increased than diminished if ptyalism be not imminent.

Nodose swellings may occur upon the tibia, scapula, sternum, and bones of the skull shortly after the appearance of the first exanthem. The lesions are tender and at times extremely painful to the touch. Usually they disappear within a few weeks. Such nodes must not be confounded with those occurring later in the disease, in which there is gummatous deposit in the part. The earlier lesions are circumscribed areas of hyperæmia with slight exudation into the periosteum, but no new cell formation.

Late lesions of bone occurring in syphilis have been classed by Lancereaux as follows:

(*a*) Inflammatory osteo-periostitis;
(*b*) Gummata;
(*c*) Dry caries.

Such lesions may occur at any time after the sixth month and as late as the twentieth year. Any bone in the body may suffer. The tibia, ulna, sternum, scapula, clavicle, and the bones of the cranium, of the nose, and of the face, suffer most frequently. One bone only may be affected at a given time or a number may suffer simultaneously or in succession.

Inflammatory Osteo-periostitis.—The lesions occurring in this form of bone syphilis are true nodes. Any of the bones may be affected, the superficial ones, such as the tibia and bones of the skull, most frequently. The periosteum and superficial layers of the bone are the parts attacked. The process begins in the connective tissue of the part and consists of inflammatory swelling, with the production of numerous embryonic cells. The bloodvessels of the Haversian canals e involved in the process, and the canals are enlarged and filled ith a plastic exudate resembling bone-marrow. There is considerle determination of blood to the part. Thickening of the tissues ccurs with the formation of a distinct tumor involving the periosteum l the parts of the bone immediately beneath. In size the tumor aries from a pea to a walnut, and is soft and doughy to the touch. he overlying skin is freely movable and is not reddened in the earlier ages of the lesion. The swelling is exceedingly tender upon pressure, d is usually the seat of a dull, continuous, grinding sensation, very ble to be intensified at night when subjected to the warmth of the ed. If the node occur upon the inner table of the skull, it is apt to roduce continuous and severe headache or nervous symptoms of considerable gravity.

The nodes, unless subjected to appropriate treatment, enlarge rapidly, he skin becomes red and adherent, the tumor softens, breaks down, and inally discharges upon the surface, with the production of a deep carious ulcer. Dead bone comes away at frequent intervals. The ulcer runs a sluggish, indolent course, after which the cavity closes with the formation of a depressed cicatrix surrounded by a hard bony ridge. At times the nodes do not undergo ulceration, but are converted into new bone extremely dense and hard in its organization. These growths are persistent and are known as exostoses. Such exostoses may be found in the periosteum, and they are freely movable upon the bone beneath. Later they may become attached to it.

Gummata.—Gummata are found in and underneath the periosteum, within the bone substance, and in the medullary canal. The long bones, bones of the skull and face, the ribs, and the bones of the fingers and toes, are most frequently affected. Gummata occurring early in the course of the disease are far more apt to be numerous than when developing late. They form rapidly and are extremely painful, the pain being nocturnal in character. When involving the periosteum, gummata can be felt as moderately firm tumors varying in size from a pea to a walnut. The neoplasms may soften, break down, and discharge outward with the production of typical degenerate syphilitic ulcers, or they may undergo resolution and absorption without the production of such lesions. In the long bones gummata are found most frequently within the medullary canal. The bone enlarges either locally or throughout the greater part of its extent. The Haversian canals entering the cavity become distended with the degenerated, cheesy products of the gummatous lesion. The pain is intense, continuing with unabated fury both day and night. The process ends by absorption of the gummy material or the production of carious bone. Calcification may take place.

In the flat bones of the skull the process is somewhat different, owing to their peculiar anatomical structure. The diploë is the part that is here most frequently attacked. The gummy deposit may be so extensive as to separate the tables, one or both of which may become carious. Necrosis of the inner table gives rise to serious brain symptoms. In the outer table sequestra are frequently formed and removed by ulceration. Destruction of scalp tissue occurs and a deforming cicatrix results.

Dry Caries.—This affection is declared by Virchow to be due to syphilis alone, and is found most frequently attacking the frontal and parietal bones. The process begins as a gummatous deposit about one of the vertical vascular channels in either table of the bone affected. Destruction of the bony tissue about the canal takes place. The gummy substance disappears by absorption and a depression in the skull results. If both tables be involved at diametrically opposite points, perforation of the cranium may follow. The skin is not involved, there is no suppuration, and no sequestrum is ever formed.

Syphilis of the Joints.—Pains in and about the joints are frequent and early in syphilis. These are not referable to any organic change in the part, but are due to the toxins of syphilis circulating in the blood. Later in the disease a true synovitis may develop. This inflammation is characterized by slight pain, impairment of motion, and effusion of fluid into the joint capsule. The joint enlarges slowly. There is thickening of the fibrous parts due to hyperplasia of their elements. The synovial membrane may become the seat of circumscribed gummata or of diffuse gummatous infiltration. The joint becomes tumid, hot, and tender to the touch. Pain is severe, and is worse at night. If unchecked, the thickening becomes permanent and there is more or less loss of motion. Complete ankylosis does not often take place, and ulceration with the formation of sinuses is unusual. The knee joint is the part most frequently affected. The diagnosis depends upon the patient's history or the discovery of evidences of syphilis elsewhere in the body. Treatment is by internal administration of the iodides and mercury, with rest of the parts affected and light mercurial inunction of the joints. Dry heat to the part is frequently grateful.

Syphilis of the Nervous System.—The nervous system may be affected by syphilis at any time in the course of the disease after the development of constitutional symptoms. Serious lesions, however, are not apt to occur early. More often they are delayed until an extremely late period, as the end of the first or second decade. Men are more apt to suffer than women, owing to the greater care, overwork, and worry that they experience. Usually the victims of nervous syphilis are individuals not yet past middle life. The belief is current that nervous affections are prone to develop in cases exhibiting but few if any of the earlier manifestations of the disease. This statement, however, lacks confirmation. It will probably be found that owing to the mildness of the early symptoms proper treatment was neglected or delayed, and the disease thereby allowed to establish itself thoroughly in the system.

At the time of the first eruption many patients complain of severe headache. This is due not to the development of organic lesions in the brain, but to the circulation in the blood of toxins produced by the syphilitic virus. These headaches are comparable in their nature and origin to the osteocopic and muscular pains experienced at the same time. They are often severe and productive of great distress. Under appropriate treatment they usually disappear in a relatively short period of time. If no mercurials have been administered previously, a tenth of a grain of calomel may be given every hour until relief is obtained or until signs of ptyalism begin to appear. This is the readiest and [illegible] They are usually [illegible] development of [illegible] accompanied by [illegible] internal capsule, and [illegible] affections of these parts are more apt to be [illegible] in some form of arterial disease. The middle cerebral artery or some one of its branches suffers the most frequently, either in the form of a specific endarteritis or periarteritis. Occlusion of the bloodvessels by thrombi may take place, or the vessel may rupture and hemorrhage into the surrounding tissues result. The size of the lesion is here in no wise proportioned to the gravity of the symptoms resulting, occlusion of the smallest artery in the internal capsule giving rise to the most serious and disastrous consequences. Aneurysmal dilatations or pouches of the arterial walls may be produced by the disease. Paralysis coming on as the result of thrombosis is slow in its onset, while that caused by rupture of an aneurysm is sudden. When slow in its approach, numbness is first noted in the foot, hand, or cheek, or it may be that some slight difficulty in speech is first experienced. These symptoms increase slowly in intensity and extent until a part or the whole of one side is paralyzed. Several days may be occupied in the process. Or, when rapid, the patient, without premonition of coming trouble, suddenly finds himself unable to speak or to use hand or foot. Consciousness is not completely lost. This feature is almost typical of syphilis. The senses are deadened and mental activity is decidedly in abeyance, but the patient can still be aroused sufficiently to show by signs that he is conscious of his surroundings. Convulsions are not often present. The reflexes of the affected side are exaggerated. Recovery may be rapid, slow, or delayed indefinitely. Atrophy of the parts paralyzed is unusual, but contractures may occur.

No grouping of symptoms referable to syphilis of the brain is possible. The best established feature of such symptoms is their variability. Headache is always present. It usually begins insidiously, increases gradually, is nocturnal in character, and is usually described as grinding, boring, or hammering in nature. Gummata of the brain, if large, may give rise to all the symptoms produced by the different forms of brain tumor. In these symptoms may be included convulsions, vomiting, and optic neuritis. Occasionally syphilitic disease of the brain may be manifested in emotional or psychical disturbances, such as mental hebetude, hysteria, hypochondriasis, stupor, somnolence, dementia, or mania.

Syphilis of the Cord.—The cord is not as frequently attacked as is the brain. The trouble may begin in the bones, in the coverings of the cord, or in the cord itself. Gummata and a diffuse proliferation of the connective tissue elements are the forms of syphilitic affection most likely to occur. Symptoms arising from such involvement are manifested in exaggeration of the reflexes, loss of control of the sphincters, spastic paralysis of the lower limbs, anæsthesia or paræsthesia, lancinating pains in the back and down the thigh, and contractures.

The relation of syphilis to tabes dorsalis appears to be definitely settled. Erb, in a series of 369 cases of the latter disease, established the fact that 89 per cent. of the patients had previously suffered with syphilis. Such a preponderance cannot be regarded in any light but that of cause and effect.

The Peripheral Nerves.—Specific involvement of the peripheral nerves may occur, and is characterized by mild or severe neuralgias, by vague, indefinite sensations, by burning pains in the toes or fingers, and by paræsthesia of limited or extended areas of the skin. The sensations produced are sometimes distressing in the extreme, and are apt to increase as the disease progresses. The symptoms are often rebellious treatment, requiring the largest doses of the iodide to subdue n.

Syphilis of the Eye.—All of the tissues of the eye, the soft parts ut it, and the bones forming the orbit may be the seat of syphilitic tions. Owing to the delicacy and sensitiveness of the structures lved such affections are apt to be grave.

The Orbital Bones.—Gummata may form in the periosteum or in the bital bones, and by their pressure effects give rise to severe pain in ne eye, disturbances in vision, or displacement of the globe. Nodes re not rare. The bones may be affected by periostitis, osteitis, carious generation, and necrosis. The inflammation excited by such processes ay extend to the eyeball and give rise to a deep seated or superficial ellulitis. Abscess may follow with discharge through fistulous tracts the eyelids. Such [illegible]es a[illegible]quently rebellious to treatment, and ay require surgical i[illegible]ference before they can be closed. Pain is ten intense, and constitutional disturbances due to depression are someimes great. The adjacent cerebral structures may become involved.

In gummata of the orbit treatment should be prompt and energetic. Reliance must be placed upon the iodides, and they must be given often in the largest doses. Their administration should be accompanied by mercurial inunctions of the feet each night. Supportive measures are needed. The bitter tonics, iron, quinine, strychnine, cod-liver oil, and the malt extracts are often necessary to improve the general condition. Locally, fomentations of boric acid solution, as hot as they can be borne, are often grateful, or, if they are not productive of comfort, cold ay be tried. Operative measures to remove dead bone or evacuate scesses are sometimes necessary.

The Lachrymal Apparatus.—The lachrymal gland and ducts may be the seat of a chronic catarrhal process. This is usually associated with some thickening of the Schneiderian membrane or disease of the nasal passages. Stricture of the lachrymo-nasal duct is apt to follow. Attention to the patient's history with reference to a luetic taint or unmistakable symptoms of syphilis in other parts are needed in establishing the diagnosis. Treatment is by antisyphilitic measures, and in case of stricture by divulsion of the duct with large-sized probes.

The Eyelids.—The initial sclerosis may occur either upon the inner or outer surface of the eyelid. The lesion is here characterized by the same signs as when appearing elsewhere. Usually considerable œdema of the parts ensues. Enlargement of the pre-auricular, parotid, and submaxillary glands on the side affected constitutes the bubo. Chancres occurring on the mucous surface of the eyelid may interfere seriously with sight.

The early consecutive lesions may appear on both surfaces of the lids, but are not frequent. Upon the mucous surface they are produced only after the part has been irritated in some manner. Mucous patches appearing upon the conjunctiva usually follow a mild course and respond readily to treatment. Local measures consist in protecting the eye with a shade and stimulating the lesions slightly by the application each day of a mild solution of silver nitrate. One to three grains of the salt to a fluidounce of distilled water is sufficient.

Gummata may appear upon the eyelid, usually late in the course of the disease. Their site of preference is along the free border. In size they vary from a pinhead to a pea. Care must be exercised in distinguishing them from cystic or fibroid tumors, which they are apt to resemble. Gummata usually involve all of the tissues of the lid, while either of the forms of tumor noted are frequently confined to a single layer, as to the integument or conjunctiva.

The Conjunctiva.—Injection and inflammation of the ocular conjunctiva are common in syphilis and are usually accompanied by an iritis of the same eye. Two cases of chancre of the part have been reported. Consecutive lesions may occur in connection with the first skin eruption. The lesions appear as circumscribed macular spots or small papular elevations, coppery in hue and without injection. They are seldom numerous. Gummata are rare. They are found oftenest in the palpebral conjunctiva, but may develop in the ocular portion at the border of the cornea. The neoplasms vary in size from a pinhead to a pea, and are usually spherical in shape. The inner surface is often reddened, while the outer is whitened or yellowish. They are liable to terminate in ulceration. If numerous, the nodules may interfere with the nutrition of the cornea in sufficient degree, by pressure upon the lymphatics, to bring about destruction of the part and complete loss of vision.

The Cornea.—The cornea is far more frequently affected in inherited than in acquired syphilis. A diffuse interstitial keratitis sometimes appears, giving to the part a cloudy, muddy appearance. The process begins at the centre and spreads gradually to the border of the cornea, or it may follow the reverse direction, beginning at the periphery and advancing toward the centre. The affection is always chronic, lasting often for years. A true punctate keratitis may arise. In this form the lesions are pinhead sized, grayish looking deposits. They are never vascularized and never ulcerate. Gummata have been observed.

The Sclerotic.—Syphilitic affections develop here in the form of episcleritis, parenchymatous scleritis, or gummatous deposit.

Episcleritis occurs as a superficial congestion of the sclerotic. It is never extensive, though several patches may be discovered at once upon the visible portion of the membrane. The conjunctiva is usually injected at the same time, and in a measure obscures recognition of the process in the sclerotic. There is but little distress accompanying the condition. Parenchymatous scleritis is deeper and far more severe. Exudation is marked. The conjunctiva is swollen and elevated. An iritis usually accompanies it. The pain may be light or severe. The process is always chronic. Atrophy and thinning of the tissues may follow, but ulceration never takes place. Gummata developing in the sclerotic appear first as small reddened, interstitial deposits. If unchecked in their course, they enlarge, extend into other coats of the eye, and may go on to complete destruction and removal by ulceration of the eyeball.

The Iris.—Inflammation of the iris due to syphilis is an exceedingly common affection. It appears early in the course of the disease, usually shortly after the subsidence of the exanthemata, but it is by no means rare at later periods. One eye only may be involved or both may suffer in succession or simultaneously. Recurrences may happen.

The patient first notices uneasy sensations or decided pain in the eye;

light is distressing to the organ; there is inability to see clearly, and epiphora results. Inspection shows the pupil small and sluggish in its reaction to light, and of a dull hazy color; the iris is discolored and slightly swollen; the conjunctiva is lightly or deeply injected; the lids are œdematous, and there is more or less lachrymation. As the result of posterior synechia the iris may become attached to the crystalline lens.

Serous iritis may give rise to exudation into the anterior chamber of the eye. The aqueous humor then becomes muddy and semigelatinous in consistency. The iris and lens are pushed back by the exudate, and sight is seriously interfered with. Nodular lesions may occur in the iris or on its surface, due to organization of the plastic material furnished by the inflammatory process. The membrane may be thickly covered with these bodies, and by their means become firmly attached to the capsule of the crystalline body. In such cases the iris exhibits the convexity of the lens.

The prognosis is good if treatment be begun before adhesions have formed. Rest, exclusion of light by means of a shade or colored glasses, and freedom from worry are essential measures in treatment. Antisyphilitic medication must be continued, but it is not often of value to push it much beyond the average dose. Local measures are of the greatest importance. Complete mydriasis must be produced and continued until the process is at an end. Two to five drops of the following solution should be instilled into the eye three times each day until the pupil is widely dilated:

℞. Atropinæ sulphatis, gr. j;
Aquæ destillatæ, ℥iv.—M.
Sig. Two to five drops in the eye three times a day.

Pain may be lessened by the addition of an eighth of a grain of morphia to the above solution or by the use of warm fomentations.

The Ciliary Body.—Syphilitic cyclitis or inflammation of the ciliary body is a somewhat rare but exceedingly grave affection. Owing to the anatomical location of the structure, the signs displayed in its affections cannot be observed by the naked eye nor by the aid of the ophthalmoscope, and reliance must be placed upon the subjective symptoms alone in determining the diagnosis. The affection may be serous, plastic, or gummatous. Its development and course are marked by severe pain, visual disturbances, ciliary injection, more or less diminution of tension, and serous exudation into the vitreous humor, obscuring or completely destroying vision. Usually the iris and choroid are implicated in the process, and the affection is then designated an irido-choroiditis. When the iris is not involved it is often retracted toward the part of the ciliary body affected. Such retraction frequently results in considerable deepening of the anterior chamber. Particles are visible floating in the vitreous humor. Minute deposits on the membrane of Descemet can be detected. The aqueous humor may become dark and turbid. Glaucoma is a frequent result of posterior synechiæ.

Gummata may extend into the ciliary body from the iris or develop in it primarily. Atrophy of the body usually results after gummatous infiltration.

The Choroid.—Choroiditis is next in frequency to iritis as a syphilitic affection of the eye, and is often associated with it. Two forms have been noted, differing in the location of the trouble rather than in the peculiarity or severity of the symptoms manifested. The first form is confined to the anterior portion of the choroid and is always accompanied by an iritis. The second affects the posterior portion of the membrane only. In either case there is exudation into the posterior chamber with resulting cloudiness of the vitreous humor. Flocculi floating free in the humor in the anterior part of the chamber are visible. Reticulated bands, appearing like cobwebs, may be formed by the plastic exudate. Small yellow specks can be seen with the ophthalmoscope upon the fundus or upon the wall of the posterior chamber. Atrophy of the cell elements at the place where these bodies are situated is apt to follow. The retina is frequently affected in conjunction with the choroid. The optic nerve usually shows a hyperæmic condition. True gummata are not known to appear in the choroid. Choroiditis occurs late in the course of the disease and usually in patients past middle life.

The Retina.—Syphilitic retinitis occurring without previous implication of the choroid is rare. One or both eyes may be affected. Subjective sensations consist of slight pain, dimness of vision, photophobia, flashes of light, slight lachrymation, and night-blindness. The retina appears as if obscured by a veil, the retinal vessels are hyperæmic, the fundus is indistinct, and the disk engorged. Loss of vision is slight or marked in degree. The affection may be confined to the fundus and the parts in the near neighborhood, or the peripheral portion of the retina may alone be affected. Syphilitic retinitis may be acute, subacute, or chronic. Vision is usually spared, though it may be greatly diminished. A peculiarity of syphilitic retinitis is that it is apt to occur when there are no other symptoms of the disease manifested elsewhere in the body. Reliance must be placed upon the history in such cases. Early recognition is essential to its successful treatment. Mixed treatment is indicated, either by combination of the iodide and the mercurial in solution, or, better, by the administration of the iodide internally and the use of the mercury by inunction.

The *optic nerve* may be affected either within the orbit or within the cerebral tissue. The inflammation develops usually in connection with retinitis. The symptoms presented are those of choked disk. There is engorgement of the vessels; the nerve is greatly swollen and infiltrated; its color is red or reddish gray, and its retinal border is wholly obliterated. Usually but one nerve is affected. Partial loss of sight often results. Only rarely does complete blindness follow.

Syphilis of the Ear.—The ear is not often the seat of syphilitic invasion, but when attacked, especially in its deeper structures, it is apt to suffer severely. Chancres due to kissing or biting are met with occasionally upon the external ear, and one case of chancre in the meatus has been noted. In the early stages of the disease the integument of the auricle may display any of the consecutive lesions incident to that period. At a later stage the substance of the lobe may become the seat of gummata. Such deposits may occur within the lobule or upon either surface of the cartilage, and the affection is apt to pursue a rapid and de-e course. Removal of a large part of the lobe may be effected. perficial ulcerations result from gummatous nodules in the skin.

Early consecutive lesions occur within the canal. They may be ist or dry and at times give rise to a tormenting pruritus. A dry m of seborrhœa developing in the part is sometimes seen in early ilis. The accumulations of sebaceous material may be sufficient to tually plug the passage. Intractable ulcers may appear within the lls of the canal. The ulcers are usually painful and productive of e discharge. Exostoses occur at the meatus, but some doubt exists to their being due to syphilis. The bony growths are not distin- ishable from similar lesions occurring in individuals free from the ease. Condylomata are by far the most frequent form of syphilitic esion found in the meatus. The affection occurs with greatest frequency in the early stages of the disease, and severe ulceration is apt follow. The lesions begin as dry papules the size of a millet seed nd enlarge to that of a pea. The papule becomes moist, the epithe- um is macerated and removed, and a typical secreting vegetation mains. Considerable pain attends the development of the lesions. nnular contraction of the meatus due to cellular infiltration in the rue skin may result in partial deafness.

Macules and papules may develop on the membrana tympani. If ulceration of the lesions takes place, perforation of the membrane is apt to result. Small gummata have been described as occurring in this structure. Affections of the tympanum are not well understood. Its intimate relationship with the naso-pharynx by means of the Eustachian tube makes it liable to participate in the troubles arising in that region. This usually happens in the form of a diffuse catarrhal inflammation of the lining membrane of the cavity, with closure of the tube and the production of partial or complete deafness. This form of serous inflammation is frequently seen in children suffering with hereditary syphilis. A true suppurative inflammation due to syphilis may arise. It is distinguishable in no wise from suppuration of the middle ear due to other causes, save that local treatment has little or no effect upon it, while it responds readily to antisyphilitic measures. A small-celled infiltration of the parts may occur as an independent affection or following one of the above described forms of inflammation. It gives rise to considerable thickening of the walls, and may produce ankylosis of the ossicles. Symptoms of trouble taking place within the middle ear are declared in diminution or complete loss of hearing, earache, suppuration, and discharge.

Little is known regarding syphilitic affections of the labyrinth. Thickening of the lining membrane owing to a hyperplastic inflammation of the parts may occur. Gummata have also been found. A sensation of ringing in the ears, vertigo, and deafness are the chief symptoms.

PATHOLOGICAL ANATOMY.

The pathological anatomy of syphilitic lesions is, with very few exceptions, not distinctive. Microscopical study of the lesions shows, in the same manner as does the clinical study of the disease, the imitative faculty of syphilis. The structural features of syphilitic neoplasms in all essential respects are like those seen in a multitude of lesions due to other morbid processes. Yet here, as in their grosser features, these changes present some characteristic appearances that reveal to the eye of the trained pathologist their true nature. The imprint of syphilis is upon them.

The most characteristic lesion of syphilis is the gummy tumor. It is not confined to any stage of the disease, but occurs either early or late in its course. Microscopical examination of such a tumor in the earlier period of its development reveals a circumscribed or diffuse mass of embryonic cells enveloped in a gelatinous basement substance and surrounded by a hyperæmic area. Epithelioid and giant cells sometimes appear. The cells are of a low order of organization and exceedingly fragile. Within the hyperæmic zone first formed a free development of connective tissue takes place, forming an apparent envelope for the embryonic mass within. From this envelope connective tissue processes invade the tumor substance and radiate into the surrounding tissues. Infiltration of the newly formed connective tissue with spheroidal and epithelioid cells takes place. New formed bloodvessels ramify freely in the mass, and there is a considerably increased flow of blood to the part. Enlargement of the neoplasm may be rapid or slow and by peripheral extension. It will be seen from the description thus far given that the lesion is not essentially a tumor in which there is a new growth occurring, but a neoplasm arising from a hyperplastic inflammation and belonging distinctively to the granulation type.

A gumma may disappear at any stage of its early development by resolution, absorption of its products taking place, or it may and does most frequently undergo cheesy degeneration. When this happens one or more necrotic points first appear within the substance of the nodule. These enlarge, become fused, and in time occupy the greater part of the tumor. The mass now appears as if composed of finely grated cheese pressed closely into a compact body. A wall of granulation tissue forms about the cheesy mass. This product of coagulation necrosis may be removed by absorption, or ulceration with destruction and sloughing of the nodule may follow. A cicatrix then results.

A second feature of syphilitic inflammation that is more or less typical in its nature is the frequency with which the process invades the vascular structures. The arteries show the specific inflammation in its completest development. As the result of the process infiltration of the walls of the vessel with small round or polyhedral cells takes place, producing an appearance that has been likened to the arrangement of the coat-sleeve about the arm. This infiltration occurs chiefly within the perivascular lymph spaces and between the coats of the artery. Considerable thickening and rigidity of the walls results. The process may be localized or extended throughout considerable areas. The product may be absorbed, but more often results in the formation of fibrous connective tissue, with the production of a limited arteriosclerosis. The vessels in the near neighborhood of the chancre are affected early.

The initial sclerosis in view of its well defined clinical aspects ought to present definite structural features. This, however, is not the
Its minute anatomy is not definitely characteristic. The changes

ed are those liable to occur in any low grade of inflammation. ere is an abundant development of small round cells within a more less dense connective tissue stroma. The parts are freely invaded by ucocytes. Giant and epithelioid cells sometimes occur. Proliferation onnective tissue elements takes place. The small bloodvessels eng the part display the above described coat-sleeve infiltration of r tunics. This latter feature is continued along the vessels to rts at some distance from the initial lesion. The newly formed connective tissue shows a tendency to persist unchanged for some length of e, but is finally absorbed. The induration of the chancre is caused dense infiltration of the connective tissue spaces with cells and by ema of the corium and epidermal layers at the borders of the lesion. is also probable that the syphilitic poison exerts a specific influence n the lymph of the part affected, and that this action of the virus is tly responsible for the ir[illegible]at[illegible] that takes place. The cells deloping in the part vary but [illegible] in size at first, but later many of them ome much enlarged and oftentimes multinuclear.

The earlier lesions of the skin, such as macules and papules, present no structural features that distinguish them from like lesions produced by low grades of inflammation not syphilitic. There is congestion of the corium with exudation into its parts, and a resulting hyperplasia of the epidermis. Pustular lesions present a torn condition of the epidermal structures, with partial or complete destruction of the corium and a mingling of the products of necrosis with blood and leucocytes. They are in no wise distinguishable from the pustules occurring in other diseases. Lesions of the mucous membranes have the same features as those presented in like lesions appearing upon the surface of the skin. In the lymph glands infiltration of the vascular channels with spheroidal and epithelioid cells appears to be the chief pathological process.

The free production of new connective tissue is a characteristic feature of the syphilitic process. This occurs in connection with the development of many of the different lesions or as the result of their disintegration and resolution. This tendency is particularly well defined in the nervous system, and especially late in the course of the disease. It is undoubtedly the element that makes syphilis an etiological factor in the production of tabes dorsalis.

DIAGNOSIS.

Early recognition of the chancre is chief in its importance in the diagnosis of syphilis. Such recognition depends upon several factors, no one of which can be omitted with safety. First and of greatest importance is the history with reference to the time of suspected infection. Sores appearing within ten days after exposure to a possible source of infection are probably not syphilitic in nature. Those occurring later than ten days, and especially at about the end of the third week, are to be regarded with suspicion. Reference must be had, in determining the length of time that has elapsed between contamination and the appearance of the sore, to records not only of the last, but of previous indulgences in sexual intercourse. A sore may be found upon the genital organs shortly after coitus that in reality had its origin some weeks previously in a similar exposure. The production and examination of the person suspected to be the source of the trouble is always a desirable, but often an unpleasant and impossible, means of verifying the diagnosis.

The physical characteristics of the lesion furnish another group of symptoms useful in establishing a diagnosis. Oftentimes these features are the only evidences obtainable upon which to base conclusions. The initial lesion of syphilis is usually single, in contradistinction to the lesion of chancroid, which is almost invariably multiple. The inflammation exhibited in chancre is not so intense nor acute as in chancroid. The chancre is nearly always indurated, the chancroidal lesion is never so. It must be remembered, however, that in early stages of chancre the induration may be so slight as not to be perceptible, and that in some regions, as in the vagina, it may never appear. It should also not be forgotten that the use of caustics upon a simple lesion may produce a condition simulating very much the indurating œdema of chancre. Inquiry with reference to the previous use of such applications is essential. It is an unwise procedure for the practitioner to be positive in his statements concerning any sore upon the genital organs in respect to which he must base his conclusions alone upon the physical signs presented by the lesion. The better practice by far is to wait for more definite symptoms. These are soon manifested in case of chancre by enlargement and induration of the neighboring lymph glands. When the sore is seated upon the penis the glands in both groins are enlarged. Rarely but one inguinal region shows this symptom. This, however, need not be confused with the enlargement shown in chancroid. In chancroidal bubo inflammatory phenomena speedily appear; the gland becomes painful and boggy to the touch, the skin reddens and suppuration occurs; while the bubo of chancre remains firm and movable underneath the skin, is not painful, and, unless complicated by chancroid, never suppurates.

In the case of men presenting genital lesions there should be free exposure of the body surface. Before examination of the sore is made it should be the rule to pass the finger-tips firmly over both inguinal regions. If any enlargement of the glands has taken place, it can be readily noted. If the investigation of the groins be made thus early, it will not be neglected, as is apt to be the case when the fingers have become soiled in handling the chancre. To search the inguinal region first is a valuable procedure in every form of venereal disease. Oftentimes in doing so a hint of trouble is obtained that otherwise might not be suspected. This is frequently the case in blennorrhœa accompanied by chancre of the urethra. After examination for bubo has been made scrutiny of the sore should follow. The lesion should be freely exposed and cleansed of all secretions. If more than one sore is present, each should receive the same careful survey. The physician need not hesitate to handle the initial sclerosis between the thumb and fore finger if the skin covering these parts be intact and sound and the hands be washed immediately afterward.

Next in order is inspection of the body surface. This should be done in a clear, strong light, and the search for signs of the disease should be thorough and complete. Syphilodermata usually appear first r the anterior surface of the chest and abdomen, but they may arise where before developing in these regions. In examining the body ne should be made of scars and relics of former trouble. Of especial lue are cicatrices in the groins as furnishing evidences of previous nereal disease.

In the case of women greater delicacy must be exercised in making such an examination. Women are apt to inspect the surface of eir bodies with greater care and frequency than are men, and their tements with reference to any eruption can be given fuller belief. nfirmation, however, should always be sought, and this can usually accomplished by exposure of a portion of the body only at a time. sually, women will submit the part affected to the physician's inpection without marked objection.

In general, it should be remembered, in distinguishing early syphiloermata from other eruptions, that the syphilitic lesions are usually symmetrical in development, extensive in distribution, not apt to be the seat of subjective sensations, and are usually accompanied by mucous patches in the mouth and throat, by loss of hair, and by other symptoms of syphilis.

The erythematous syphiloderm is to be distinguished from the rashes appearing in the eruptive fevers by its deeper color, by its indolent character, by the involvement of the palms and soles, and by the absence of catarrhal discharge. If fever is present, it seldom rises as high in syphilis as in the exanthemata, and is apt to persist for a longer time. In syphilis relics of the initial lesion can usually be found or a history of the chancre's recent existence elicited. Osteocopic pains, sore throat, mucous patches in the mouth, and alopecia are usually present. Erythematous eczema is usually less extensive in its involvement of the skin, and is productive of intense itching, while the lesions of syphilis give rise to no discomfort. In eczema the color is a brighter red and moisture of the surface appears sooner or later. In tinea versicolor the patches are tawny in color, and are found most frequently on the surface of the chest. The microscope shows the characteristic fungus. Drug eruptions are accompanied by a marked degree of discomfort, and appear in unusual sites and forms. A history of some ingested medicament can usually be obtained.

Papular syphilodermata are easily distinguished from papules occurring in other diseases by their peculiar forms and distinctive groupings. Papules in eczema are frequently surmounted by a minute vesicle or covered by a blood-crust indicative of the scratching by which relief is sought from the tormenting pruritus. On the hands and feet syphilis confines its attacks to the palmar and plantar regions, while eczema involves both anterior and posterior surfaces. Ringworm can be distinguished by the aid of the microscope, the tricophyton being readily discoverable. In psoriasis the glistening, pearly white scales surmounting the lesions and the chronic sluggish action of the process are distinguishing features.

The pustular syphiloderm must not be confused with the lesions of acne, smallpox, or the eruptions produced by the ingestion of potassium iodide or potassium bromide. In acne the evident involvement and limitation of the process to the sebaceous glands at once determines the nature of the disorder. Comedones also are always found mingled with the pustules. The fever and severe constitutional symptoms of smallpox exclude syphilis. Knowledge that the bromine and iodine compounds have been ingested is usually sufficient to establish a distinction in the case of bromic or iodic acne. The pustules of syphilis show a well defined areola, while ulcerative lesions are nearly always present.

The diagnosis of late manifestations of the disease must depend upon the history, upon the typical grouping, upon the usually sluggish action, and upon the destructive course of the lesions.

TREATMENT OF SYPHILIS.

The proper treatment of syphilis takes into consideration the improvement of the patient's general health by hygienic measures, as well as the medicinal attack to be made upon the disease. Neither can be neglected with safety, and only as they are made to supplement and assist each other can the best results of treatment be hoped for. Attention must be directed early to the patient's habits and methods of life, and if these be found faulty or vicious they must be corrected. Previous periods of ill health should be made the subject of inquiry, and provision be made for their recurrence or resulting sequels. If the patient be surrounded by unhygienic conditions or engaged in business calculated to produce ill health, a change of location or of employment should be urgently recommended. Hopefulness and cheerfulness on the part of the person affected must be secured if possible. Despondency, often seen in patients of this class, frequently nullifies the physician's efforts. Upon the untiring watchfulness with which the practitioner guards these factors depends in a large part the favorable or unfavorable outcome of the therapeutical measures he institutes.

Hygienic Measures.—Everything looking toward the maintenance of the patient's health on the highest plane possible is of utmost value in the treatment of syphilis. As in the treatment of disease in general, so in syphilis it may be affirmed with truth that the patient presenting and maintaining a sound body is in the best condition to resist the encroachments of the malady. To the end of securing such a condition proper nutrition of the body is chief in importance. Any conditions or disturbances interfering with digestion or assimilation must be removed as early as possible. The diet should be ordered in such manner that there will be no return of the trouble, while ample nourishment is secured. In arranging the diet reference must be had to peculiarities of the patient's case, such as extreme plethora or anæmia. In general it may be said that a person suffering with syphilis needs a generous diet of nutritious and easily digestible articles of food which have been well and simply cooked. Meals should be had at regular intervals, and should be eaten slowly and with care in thoroughly masticating the food. Very hot or very cold drinks or dishes, as well as highly seasoned foods or an undue amount of sweets, should be interdicted. Fresh fruit, fresh vegetables, and fresh meats if well cook may be permitted in abundance. Tea and coffee, if drunk spar and after the meal, do no harm. Lemonade may be taken if ag

It is well always to prohibit the use of alcoholic beverages, not because the moderate use of the milder stimulants is harmful, but to avoid danger of their abuse on the part of the patient. A majority of ndividuals suffering with syphilis are persons who have indulged their tites with reference to alcohol freely, and limitation of its use is to of decided advantage. When permitted, drinking should be llowed only with the meals, and then in small quantities of the lighter wines or liquors, such as claret or Rhine wine, and beer, ale, or porter. Drinking at a bar should never be tolerated. In weak and cachectic subjects alcoholic stimulants are frequently indicated, and the practitioner need not then hesitate to use them.

A moderate amount of daily exercise in the open air is essential. The regulation of this must be determined by the patient's habits and ccupation. For persons eng in sedentary pursuits at least one hour should be devoted each y, when the weather will permit, to walking, rowing, or riding. O oor sports that do not call for too great exertion, such as tennis an golf, are of decided value both in the xercise they furnish and the d rting influence they exert upon the mind. Fatigue of both body and mind should be strictly guarded against.

Proper bathing of the body needs careful attention. Hot baths, notwithstanding their vaunted specific properties at certain springs and resorts for the cure of the disease, are in the early stages of the malady productive of a great deal of harm. The popular Turkish and Russian baths, as well as hot tub baths, should be strictly prohibited. In their place sponging of the entire surface each day with cool or, in the case of weak and anæmic patients with tepid, water should be ordered. If a small quantity of salt be added, as a handful to two or three gallons of water, the result will be found decidedly exhilarating and refreshing. Friction of the surface after the bath with a flesh brush or coarse towel should not be omitted. The bath is best taken in the morning immediately after rising. If such a course be pursued, many of the severer syphilodermata will never make their appearance. Bathing of the body in the case of women should be stopped at the time of the monthly period.

Tobacco in all forms is decidedly injurious, and frequently produces lesions that give rise to great discomfort. When its use is persisted in, it is apt to excite severe ulcers, mucous patches, and fissures of the lips and parts within the mouth cavity. Tobacco also exerts a vicious influence upon the system, interfering in a decided manner with the best results to be obtained from therapeutical measures. Its use, either by chewing or smoking, should be abandoned promptly and completely at the outset of the disease.

Especial attention should be given to the care of the mouth and to the protection of the throat. Thorough cleaning of the teeth by means of the toothbrush and tepid water should be attended to after each meal. The brush used should be sufficiently firm to remove all particles of food clinging to the teeth, but not harsh enough to wound the sensitive mucous membrane covering the gums. Other sources of irritation, such as holding a pipe or cigar between the teeth, chewing a toothpick, gum, or other substance, should be prohibited. Decayed teeth should be extracted or have their cavities filled; sharp projections must be rounded off and accumulations of so-called tartar be thoroughly scraped away by a capable dentist early in the course of the disease. The throat must be kept warm by the use of ample coverings in cold weather, and the wearing of a beard by men should be encouraged, both for the protection it affords and to guard against the ill effects produced by close shaving.

The scalp needs proper attention as well, in order that loss of hair may be averted. Indiscriminate washing of the head with each ablution of the face is harmful. In its stead thorough cleansing of the part with warm water and a good toilet soap, such as the Rieger or Sarg fluid soap, should be secured once in ten days or two weeks. After each washing the hair should be well dried, and a few drops of oil of olives or sweet almonds should be thoroughly applied. Polishing of the scalp with a moderately stiff brush should be practised each morning. In men clipping of the hair is not needed if the individual does not prefer to wear it in that manner. Singeing is decidedly harmful and should never be permitted. The crown of the hat should be perforated to permit as free ventilation of the scalp as possible. In women the hair may be worn in any form suited to the individual, provided that there be no tension exerted upon the filaments. The use of the curling iron should be prohibited.

Treatment of the Chancre.—The belief that syphilis can be aborted by excision of the initial lesion is entertained now by only a limited number of syphilographers. Admitting that the poison is confined at an early stage to the chancre, its accompanying glandular enlargements and the intervening lymphatics, removal of all the foci established therein, even with great loss of tissue and severe mutilation, can hardly hope to be effected. Excision of the chancre can only be justified when its exposure on the face or other external part by betrayal of the patient's condition seriously interferes with social or business engagements. Its removal then must not be with any hope of staying the subsequent course of the disease.

That course of treatment is best for the chancre which seeks to remove all sources of irritation from the lesion and to keep it in a thoroughly aseptic condition. The simpler such treatment the better are the results obtained. The chancre should be thoroughly cleansed at frequent intervals with soap and warm water, after which the sore should be dried and bathed with a saturated solution of boric acid as hot as can be comfortably borne by the patient. This should be done at least twice a day at times best suited to the patient's convenience. After bathing with the boric acid solution the part should be dried and dusted freely with some unirritating antiseptic powder, such as boric acid in combination with talc or starch in the proportion of one to four, aristol, iodol, europhen, calomel, or iodoform if its odor be not offensive to the patient. Other solutions of value when boric acid is not at hand are permanganate of potassium in the strength of one grain to the fluidounce of water, bichloride solution 1 : 20,000, or a $\frac{1}{2}$ to 1 per cent. solution of carbolic acid. These should always be used warm. Chancres of the penis or finger may be conveniently immersed in such solutions contained in a cup or tumbler and allowed to remain for ten or more minutes at a time. If the lesion be productive of much pain, as happens sometimes in the case of mixed chancre, such immersion may be continued for hours with great advantage and comfort to the patient. Chancres of the finger may be protected by a light bandage neatly applied, but in general no dressing is needed for the lesion in other parts. A bandage should never be wrapped about the penis. Here a square of muslin or unbleached sheeting may be fastened in the form of an apron to the under side of the shirt, and the parts then be gathered loosely about the penis. In this way the underclothing need not become soiled with the secretions from the chancre. All dressings used about the lesion or becoming soiled in any way with its virus should be destroyed by burning. Chancres of the tongue, tonsil, and mouth cavity should be painted lightly once each day with a solution of silver nitrate in the strength of ten grains of the salt to an ounce of distilled water. If chancre of the lip or external part shows signs of suppuration, it should be touched with an applicator, made of a toothpick and a bit of cotton, dipped in the following solution:

℞. Hydrargyri chloridi corrosivi, gr. j;
Tincturæ benzoini, ℥j.—M.
Sig. External use.

This solution is decidedly stimulating and should not be too freely used.

Chancres of the os uteri and vaginal cavity are best treated by the use of boric acid douches as hot as can be borne. The permanganate of potassium and bichloride solutions can be used here as well. The douching should be practised at least once in the day. Frequent applications of the nitrate solution, used as in the case of mouth lesions, help to promote healing and resolution of the sore. Tampons are not often needed.

Œdema of the penis calls for its prolonged immersion in a hot borated lotion, and subsequent elevation of the organ along the groin. This can be accomplished easily by putting a broad band of muslin firmly about the abdomen and then passing another between the limbs and fastening it before and behind with safety pins. To those who can secure it a jock-strap furnishes a support that can be more easily and quickly applied. If the lymphatics become swollen and tender, the application of the following ointment after sponging the parts affected with hot water will usually give prompt relief:

℞. Tincturæ belladonnæ, ♏x;
Extracti opii (aqueous), gr. ij;
Vaselini, ℥ss.—M.
Sig. External use.

Care should be exercised in the use of the above ointment, as the mydriatic effect of the belladonna may be readily produced.

Systemic Treatment of Syphilis.—When to begin the systemic treatment of syphilis is a question concerning which a great diversity of opinion exists among syphilographers. This, however, is not the place to give in detail the different views entertained nor to promote by a prolonged discussion any one particular course of procedure. Success does not depend so much upon the time that antisyphilitic measures are begun as upon their intelligent direction after once being instituted. It is believed that what is said in the following pages will apply as well to treatment first employed after the eruption of the syphilodermata as when the course is ordered at an earlier stage.

Treatment should be commenced as soon as a positive diagnosis of syphilis can be made, and it should not under any circumstances be instituted before such time is reached. If the practitioner is in doubt, he should wait. If he is to guide his patient through the disease to its successful termination, his own mind must not be clouded by a doubt as to the nature of the malady he is combating. It will be an act of wisdom on his part to err on the side of too great caution, rather than to begin mercurial medication upon insufficient grounds. Treatment once begun is apt to modify the nature of the symptoms manifested and to prevent a typical expression of the disease, so that if the practitioner be not sure of his position at the start, he has no means of verifying his diagnosis later. The result will always be a weak and ineffectual course of medication at a time when energetic treatment is productive of the greatest benefit.

The question thus turns on the diagnosis of syphilis. Most practitioners prefer to wait until the disease manifests itself in unmistakable constitutional symptoms, such as a generalized exanthem, glandular enlargement, and sore throat. If treatment be begun promptly at such time and pushed vigorously, the great majority of patients will respond readily and will make complete and good recoveries. But it is not always necessary to wait for all of the above described symptoms in order to make a diagnosis, and in so doing valuable time is often lost. As has been said elsewhere, a sore appearing at the end of a well defined incubative period, presenting the characteristic sluggishness and induration of chancre, and accompanied by typical enlargement in both groins, is sufficient to establish a diagnosis of syphilis and to warrant the commencement of systemic treatment. Experience justifies the assertion that measures thus early begun, if properly directed, result in the production of a milder and far more tractable form of the disease than is otherwise the case.

Mercury.—There is no drug comparable with mercury in the treatment of syphilis. Centuries of use have attested the efficiency of its action in checking and curing the disease. The employment of the drug, however, needs skilful direction. To the abuse, and not to the proper administration, of mercury can be traced all of the ill results with which it has been so often charged, while the charlatan has not hesitated to attribute to the action of the drug many specific expressions of the disease.

There are two methods of employing mercury—one by the way of the stomach, the other by the skin. The first is known as the *internal* method of administration, the second as the *external.* Both are valuable means, and both are equally effective in the results they produce. Their individual or combined employment throughout the course of the disease must be determined by the necessities and emergencies arising in the case.

In the internal administration of mercury the protiodide, biniodide, bichloride, blue pill, gray powder, and mild chloride are the preparations of the metal commonly employed. Of these, the protiodide is by far the most reliable and effective in the results it produces. There are few patients who cannot tolerate its action, even in very large doses, and its use can be continued for longer periods of time without apparent diminution in the good to be obtained from it. In the early stages of syphilis it is often necessary to increase the dose very largely to meet various conditions of the disease that may arise. Under such circumstances it is well to give the drug in pill form uncombined with other medicinal agents, as follows:

℞. Hydrargyri iodidi viridi, gr. xij;
Confectionis rosæ, q. s.
Misce et fiant pilulæ No. lx.
Sig. One pill after each meal.

Or use may be made of the Garnier and Lamoureux pill. This pill contains one centigram of the protiodide, and, owing to the manner of its preparation, can often be tolerated by the stomach when the drug in its pure state would prove irritating. In beginning medication one of the above pills should be given after each meal. If urgency in the treatment of the disease is demanded, as when a well developed exanthem accompanied by mucous patches and sore throat is first presented, the number of pills taken may be gradually increased until subsidence of the symptoms becomes manifest or constitutional effects of the drug begin to appear. In such increase it is well to order the patient to take one pill after each meal for the first three days. Then an additional pill is to be taken after the noon meal for the next three days, making four pills taken during each day. During the succeeding three days two pills are taken after the morning and evening meals, and but one at noon. In this way the number can be pushed gradually upward until as many as twenty or more pills may be taken during each day without the production of toxic symptoms. These large doses, however, are rarely needed and seldom reached. In general, it will be found that from six to nine pills a day are sufficient to bring the disease under subjection or to produce gastric disturbances necessitating the stoppage of further increase. During this time the patient should be under strict observation by his physician. Daily inspection of the individual should be had, and as soon as evidences of toxic action on the part of the drug are manifested the increase should be stopped and the number of pills being taken reduced one half. Toxic effects are first shown in the protiodide by increased peristaltic action in the intestinal tract. No attention need be paid to the symptoms if the number of loose stools does not exceed two or three in the day, but when they become more numerous and are accompanied by severe griping pains, it is time to stop pushing the drug. Sometimes the first effects of the protiodide appear in the usual evidences of hydrargyrism, such as softening of the gums with the formation of a red line at their border, fetor of the breath, and a metallic taste in the mouth.

If improvement in the specific symptoms has not been noted before the beginning of toxic effects, the protiodide should not be continued longer in the hope that it may prove beneficial, but it must be discontinued and some other preparation be substituted.

It is usually of decided advantage to combine a light course of mercurial inunction with the internal administration of the protiodide. A scruple of the officinal blue ointment should be thoroughly rubbed into the sole of one foot each night before the patient retires to rest. The foot should be bathed first in warm water, and afterward be thoroughly dried before applying the ointment. A light sock may be drawn on to protect the sheets from being soiled. On the following night the other foot may be treated in like manner. Between ten and twenty of these rubbings may be given as seems best to the physician. Such inunctions should be discontinued promptly if constitutional effects of the drug intervene.

Iron in some form is indicated if the patient be in any wise anæmic or cachectic. It is well always to begin its administration in small doses at the time that mercurial treatment is instituted, in order to prevent the appearance of the above-named conditions and to check in a measure the peristaltic action produced by the protiodide. The following will be found valuable:

℞. Ferri et quininæ citratis, ʒj–iij;
Syrupi limonis, f℥ij;
Aquæ destillatæ, q. s. ad f℥vj.—M.
Sig. A teaspoonful in water before two meals.

Attention should be directed early to the enlarged glands both of the bubo and those appearing later in different parts of the body. It should be remembered that these glands are foci for distribution of the virus and the products of syphilis, and that a direct attack on the seat of the disease can here be made. The integument over each gland should be sponged at night with warm water, and after drying, the following ointment should be gently and lightly rubbed in:

℞. Unguenti hydrargyri, ʒij;
Lanolini, ℥ss.—M.
Sig. External use.

If the ointment be warmed slightly before applying it to the skin, better penetration will be secured. Care should be exercised not to produce a dermatitis by its too frequent application.

With subsidence of the symptoms decrease in the amount of the protiodide taken should be ordered, until a dose is reached that will hold the disease well under control and suppress all symptoms of it. This dose should be continued steadily, with such increase or decrease in quantity as varying conditions of the disease may seem to indicate, for a period varying from one and a half to two years. The iron and the protiodide may conveniently be combined as follows:

℞. Hydrargyri iodidi viridi, gr. xvj;
Ferri et quininæ citratis, ℈iv.
Misce et fiant capsulæ No. lxxx.
Sig. One after each meal.

℞. Hydrargyri iodidi viridi, gr. xvj;
Massæ ferri carbonatis, ℈iv.
Misce et fiant capsulæ No. lxxx.
Sig. One after each meal.

above prescriptions can often be used interchangeably with considerable value, the different forms of the iron apparently agreeing well with the stomach. If at any time symptoms of the disease make their ppearance, the amount of the mercury can be increased by the taking of one or more protiodide pills with each dose.

In order to relieve the stomach of the burden placed upon it, internal treatment may be suspended at intervals of three months and a course of inunctions substituted. In general such course should not last for a longer period than two weeks, and should be followed by a return to the protiodide.

If it should be found after a thorough trial of the protiodide that success cannot be obtained with its use, or if it disagrees in any manner with the patient, its further administration should be stopped and some other preparation of mercury tried in its place. The bichloride is of decided value and can be given as follows:

℞. Hydrargyri chloridi corrosivi, gr. j–ij;
Tincturæ ferri chloridi,
Acidi hydrochlorici diluti, āā. f ʒij;
Syrupi limonis, f ℥ij;
Aquæ destillatæ, q. s. ad f ℥vj.—M.
Sig. Teaspoonful in water after each meal.

Or the above can be given after the first and last meals of the day, and a pill containing one fifth grain of the protiodide after the middle meal and at night when retiring.

The biniodide may be tried in pill form in the dose of one fiftieth to one twenty-fifth of a grain, or it may be combined in capsule with the forms of iron given in connection with the protiodide.

Calomel in doses of one tenth of a grain can be employed every hour in the day until the cathartic action of the drug is made manifest, when it should be administered less frequently.

The gray powder in pill form is sometimes serviceable when the others fail:

℞. Hydrargyri cum cretæ, ℈iv.
Fiant pilulæ No. lxxx.
Sig. One pill after each meal.

If all these methods fail, resort must be had to some one of the external methods. The method by inunction is to be preferred.

Mercury by Inunction.—This is always a valuable method of administering the drug, because it relieves the stomach of an enormous burden otherwise placed upon it, and leaves it free to perform its natural functions. The great drawbacks to the more frequent employment of mercury by inunction are its seeming dirtiness and the dislike that patients have to the labor involved in the application. When, for any reason, the stomach cannot be made to tolerate the various mercurial preparations, or when the patient does not improve under such treatment, inunctions should be employed. The hour before retiring is the time best suited for their application. The body may be divided into as many regions for the purpose as suits the practitioner's wishes or the patient's convenience, the essential factor being to rub the ointment in well. Six divisions are usually sufficient, and instructions may be given as follows. The patient is ordered on the first night to bathe well with soap and warm water the arms above the elbows, the shoulders, and the chest region above the nipple line; then to dry the parts and to rub thoroughly into them from one half to two drachms of mercurial ointment. The officinal ointment of the Pharmacopœia of 50 per cent. strength has stood the test of time and may be used with good results, but the mercurial ointment prepared by many druggists, in which the metal in the same strength is incorporated with lanoline as a basis, furnishes a preparation offering decided advantages in the ease with which it can be applied. On the following night that part of the anterior surface of the body between the nipple line and the crural angles is treated in like manner, and then on succeeding nights the following regions in the order named: the posterior surfaces of the body that can be easily reached and the buttocks; the lower limbs as far as the knees; the limbs below the knees; and lastly, the soles of the feet. After each inunction the patient clothes the part subjected to the process with some suitable garment and retires to rest. Upon the upper segment of the body the night shirt protects the sheets in sufficient manner. When the lower half is undergoing treatment a pair of drawers may be drawn on. If at any time before complete inunction of the body is accomplished the parts where the ointment has been applied show signs of irritation, such regions may be washed clean with soap and warm water and dusted with starch or finely powdered talc. If no signs of trouble appear, bathing should be postponed until the seventh night, when the entire body should be cleansed of all traces of the ointment by means of a warm bath. If needed, the entire process may be repeated, beginning on the following night, or the inunctions may be continued on the soles of the feet, shifting at regular intervals from one foot to the other.

The mouth must be watched carefully while the inunctions are in progress, and, if the gums show signs of coming trouble, the process must be stopped and a bath ordered.

Mercury by Fumigation.—This plan of using mercury is of decided value when extreme urgency in the symptoms calls for immediate action on the part of the drug. Fumigation is especially useful in those cases of extensive syphilodermata in which the lesions cannot be made to submit to ordinary forms of treatment, or when their rapid removal from the face and exposed parts is necessitated by the patient's desire for secresy. In the large cities many of the bathing establishments furnish admirable facilities for giving mercurial fumigations, and when conveniently situated it is well for the physician to make use of the advantages offered. In the country or where the patient cannot be induced to attend one of the institutions named the practitioner can [illegible] patient's own home in the following [illegible] undressed and seated upon a cane- [illegible] blanket is fastened closely about [illegible] the floor in the form of a [illegible] Underneath the chair a pan [illegible] good-sized spirit lamp. Care [illegible] in contact with the flame. [illegible] upon the edges resting on [illegible] The steam from the [illegible] of the body. As soon as the [illegible] mercurial chosen for sublima- [illegible] underneath the blanket. The [illegible] contained may be made of a [illegible] and supported upon suitable rests. [illegible] preparations of mercury best suited [illegible] used singly or with better results [illegible] a scruple to a drachm of either [illegible] combination, it is well to use [illegible] of calomel. Thus a half drachm [illegible] may be taken. The fumigation [illegible] thirty minutes if no untoward symp- [illegible] the patient becomes faint or experiences [illegible] must be stopped at once, the body [illegible] administered. It is a good plan in the [illegible] patients to give a small quantity of brandy [illegible] beginning the operation. After the fumigation [illegible] Care must be exercised in not per- [illegible] during or after the operation. Such [illegible] oftener than every second day, and [illegible] Supportive and tonic treatment [illegible] employed.

[illegible] and nasal passages is frequently [illegible] syphilitic lesions appearing in these [illegible] furnishes an elegant and easy [illegible] for such purpose. In its place a hot [illegible] used. Five to ten grains of calomel can [illegible] as the fumes rise they can be drawn [illegible] inhalation. Irritation of the bronchi [illegible] prolonging the process nor repeating it [illegible]

Hypodermic Method.—The value of this [illegible] syphilis is not definitely decided. There [illegible] give it their hearty support, but they are [illegible] the operation and the occasional disas- [illegible] its use interfere with its extensive em- [illegible] rapidity and certainty of cure can be [illegible] demands verification. Only the briefest [illegible]

[illegible] salts of mercury may be used. Cor- [illegible] the following formulae, is most fre-

℞. Hydrargyri chloridi corrosivi,	gr. ¼;
Sodii chloridi,	gr. ¾;
Aquæ destillatæ,	f ℥j.—M.

Sig. Inject from one half to one drachm every third day.

℞. Hydrargyri chloridi corrosivi,	gr. x;
Acidi tartarici,	ʒss;
Aquæ destillatæ,	f ℥j.—M.

Sig. Inject ten minims twice a week.

℞. Hydrargyri chloridi corrosivi,	gr. j;
Glycerini,	
Aquæ destillatæ,	*āā.* f ʒj.—M.

Sig. Inject ten minims daily.

Other soluble salts of mercury that may be tried are asparagin-mercury in 1 or 2 per cent. of mercurial strength; the oxycyanide, gr. xv of 1.25 per cent. of mercury; the carbolate of mercury, gr. ⅙ to ⅓; and the benzoate, mercuric albuminate, and peptonate.

Among insoluble preparations, calomel, gray oil, yellow oxide, black oxide, salicylate, protiodide, biniodide, cinnabar, sulphate, and metallic mercury are a partial list of the different forms used. The use of the insoluble salts is less satisfactory than is that of the soluble varieties. The manner in which calomel is used can be taken as the type for most of the compounds given. The salt should be first thoroughly sterilized by subjecting it for at least one hour on two successive days to the action of steam, and then employing it as in the following:

℞. Hydrargyri chloridi mitis,	gr. ss;
Glycerini,	♏x;
Aquæ destillatæ,	♏x.—M.

Sig. Inject every four days.

The amount may be increased so that two grains a week can be given.

Instead of the above formula the following is sometimes used:

℞. Hydrargyri chloridi mitis,	gr. j;
Mucilaginis acaciæ,	♏xx.—M.

Sig. Inject every four days.

In performing the operation asepsis is of the greatest importance. The site of operation must receive as thorough preparation as for any surgical operation, the hands of the operator must be absolutely clean, and the instrument and preparations used be sterilized. The injection should be made deeply into the tissues, the buttocks furnishing a favorite site. The patient should lie flat upon the belly while the operation is being performed. The needle used should be about one half longer than that ordinarily employed in hypodermic medication. Care must be exercised not to make the injection into a bloodvessel.

Hydrargyrism.—The toxic effects of mercury may follow quickly upon its first administration or appear only after the drug has been given for a long period of time and in very large doses. The first symptoms are usually manifested in soreness and sponginess of the gums. A distinct red line is formed at their border, and the mucous membrane bleeds readily. The teeth feel long, and unpleasant sensations are experienced when the jaws are brought forcibly together. There is an increased flow of saliva, the tongue is heavily coated and swollen, and the breath is decidedly offensive. These symptoms may come on slowly or rapidly. If the drug be continued, all of the above manifestations become intensified. The saliva flows in a stream from the mouth, the swollen tongue fills the mouth cavity and projects between the lips, necrosis of the jawbones takes place, the teeth fall from their sockets, there is high fever, the bones and joints ache, and pain and distress are felt in every part of the body.

Prophylaxis consists in keeping the mouth perfectly clean and removing from it every means of irritation. At the first signs of ptyalism the mercury should be promptly suspended and iron tonics be given. If severe symptoms come on, the patient must be made to remain quiet, the emunctories of the body be kept open, the diet should be nutritious and of easily digested foods, and the mouth treated with soothing lotions of myrrh and honey. The gums should be gently wiped several times a day with a bit of soft cloth moistened in the following:

℞. Tincturæ myrrhæ,
Tincturæ cinchonæ, āā. f ℥ss.—M.
Sig. External use on gums.

Lotions of oatmeal water and honey are frequently grateful, as are mild solutions of potassium chlorate. All liquids, either beverages or washes, should be gently warmed before using. If the case be carefully managed, a good recovery will usually be made. Often slight salivation is of decided benefit in the treatment of the disease.

The Compounds of Iodine.—The compounds of iodine are indispensable in the treatment of syphilis. They cannot, however, take the place of the mercurials in the general measures instituted for the relief of the disease. The field in which the iodides are found useful is limited, and their employment should be restricted within such limitations. No treatment of syphilis can be more unwise than the indiscriminate giving of the iodine salts, as is often done early in the course of the disease. There is more of truth than error in the statement that mercury cures syphilis, while the iodides but check its progress. Dependence must be placed upon the salts of mercury to eradicate the disease from the system, while the iodides are useful in bringing under subjection late symptoms that are to be regarded as sequelæ rather than actual manifestations of syphilis. The iodides are indicated in the following conditions: First, when gummata make their appearance, during any stage of the disease, in the skin or in deeper and more vital organs; second, in those cases where the patient cannot be made to tolerate mercury in any form; third, where mercury has been administered for a long period of time it is frequently of value to interrupt the course and in the mean time to give the iodides; fourth, when syphilitic lesions cannot be made to respond to vigorous mercurial treatment.

When the iodides are given according to the above indications their intelligent administration is often attended by brilliant results.

The salts of iodine usually employed include the iodides of potassium, sodium, strontium, lithium, and rubidium. Of these the iodide of potassium has the widest range of usefulness, and is the most effective in obtaining desired results. The iodide of sodium comes next in point of efficiency.

The iodide of potassium may be given in solution in teaspoonful doses containing five, ten, or twenty grains of the salt three times a day, but it is better practice to give it in drop doses of a saturated solution, as follows:

℞. Potassii iodidi, ℥j;
Aquæ destillatæ, q. s. ad f℥j.—M.
Sig. Drop doses as directed.

One drop of the saturated solution represents nearly one grain of the salt. In giving the drug in this manner its dosage can be varied to suit the conditions and necessities of the case. It is well to begin its administration in five drop doses after each meal and at bedtime, increasing the dose one drop each time or one drop in the day as the urgency of the case may demand. The increase should be pushed steadily until relief is obtained from the symptoms or until signs of iodism make their appearance. Often doses running up each to a hundred or more grains are demanded, and are well borne by the patient. The drug should be given in milk or pure water, and always after the taking of food.

Oftentimes the iodide can be tolerated better when combined with essence of pepsin, as follows:

℞. Potassii iodidi, ℥j;
Essenciæ pepsini, ℥ij.—M.
Sig. Drop doses as directed.

This represents the drug in about one third the strength of the saturated solution, and its dose must be correspondingly increased.

When a fixed dose of the iodide is to be given for an extended period of time, it may be used as in the following formula:

℞. Potassii iodidi, ℥ ss–iiss;
Syrupi aurantii corticis, f℥iij;
Aquæ destillatæ, q. s. ad f℥viij.—M.
Sig. Teaspoonful in water after each meal.

The iodide sometimes causes considerable distress in the stomach and interferes greatly with digestion when taken immediately after eating. In such cases it is well to give the following as soon as the meal is finished, and the iodide an hour afterward:

℞. Tincturæ nucis vomicæ, f℥ss;
Essenciæ pepsini, ad f℥vj.—M.
Sig. Teaspoonful in water after each meal.

The iodide of potassium should always be stopped if marked consti-ation occurs during its administration or if disturbances in the kidney rise. Measures for the relief of such conditions should be instituted, nd the use of the iodide should not be resumed until the normal func-ions of the parts have been restored.

Iodism.—The toxic effects of the iodides are more readily shown than is the case with mercury. Such results of the drug's action may be expressed in a great variety of lesions appearing upon the skin or in the production of salivation—a metallic taste in the mouth, coryza, constipation, fever, and all of the symptoms of peritonitis; or it may occasion attacks of vomiting which increase in frequency and severity, veakness, anæmia, and loss of sexual appetite. The commonest symp-om of iodism is iodic acne. The lesions appear upon the face, neck, chest, and back with greatest frequency, and are difficult to distinguish from the like symptoms of acne vulgaris. Frequently the smallest dose of potassium iodide will cause the eruption to appear, while if the drug be pushed properly the lesions will vanish. Urticaria of severe type is liable to be produced. In case of dangerous symptoms arising the iodide should always be stopped and a tonic be given. Usually all manifestations of trouble disappear readily when such a course is pursued.

MIXED TREATMENT.—By this term is meant the use of the iodide and the mercurial in combination. It is evident that the combined action of the drug can be secured in various ways. The iodide can be given internally and the mercurial externally by inunction, fumigation, or injection; the iodide can be given at one time of day and the mercurial at another, or the two can be given internally in the same dose. To the last method the term "mixed" is usually applied. This method of medication is useful in early stages of the disease, when the development of tubercles, gummata, or bone and brain lesions calls for the administration of the iodides.

If the symptoms are urgent, treatment should be begun by giving the iodide internally and the mercurial externally. In this way either drug can be increased or diminished as indications demand. When the disease has been brought well under control, the two salts may be combined as in the following:

℞. Hydrargyri iodidi rubri, gr. i–ij;
Potassii iodidi, ℥ss–ij;
Syrupi glycyrrhizæ, f℥ij;
Aquam destillatam, ad f℥viij.—M.
Sig. A teaspoonful in water after each meal.

Or,

℞. Hydrargyri iodidi rubri, gr. i–ij;
Sodii iodidi, ℥ss–ij;
Syrupi zingiberis, ℥iij;
Aquam destillatam, ad ℥viij.—M.
Sig. Teaspoonful in water after each meal.

The bichloride may be given in the same manner:

℞. Hydrargyri chloridi corrosivi,	gr. i–iij;
Potassii iodidi,	℥ss–ij;
Syrupi glycyrrhizæ,	℥ij;
Aquæ destillatæ,	q. s. ad f℥viij.—M.

Sig. Teaspoonful in water after meals.

This latter combination is often brilliantly effective, but, owing to the possibility of double decomposition taking place between the mercuric salt and the iodide, the combination is not as trustworthy as when the biniodide is used.

A valuable method of administering mercury and the iodide is to give them singly at different times in the day. The iodide can follow the morning and the evening meal in either a graduated or fixed dose, while the mercurial can be given in pill form after the noon meal and when going to bed, at which time a little food or a glass of milk should be swallowed. Neither mercury nor the iodides should ever be given on an empty stomach.

LOCAL TREATMENT.—Proper local treatment of syphilitic lesions and conditions is of great importance. By the help thus afforded repair and resolution of the parts affected may be much more quickly accomplished than when reliance is placed entirely upon constitutional measures.

In syphilis of the skin avoidance of anything that may irritate and annoy the organ must be carefully attended to. Light uncolored balbriggan or cotton underwear should be worn next to the body. Over this, if the weather be cool, the patient should wear suitable woollens, but these should never be allowed to come in contact with the skin. Tight wristbands and collars should be exchanged for articles that will not chafe the parts nor interfere with the circulation.

Usually syphilodermata disappear rapidly under appropriate systemic treatment, but if inclined to be sluggish or when, appearing on the face, the lesions betray the patient's condition, resolution may be hastened by the following measures:

The parts affected should be sponged each night with warm water, and after drying be anointed thoroughly with an unguent composed as follows:

℞. Hydrargyri ammoniati,	gr. v–x;
Balsami Peruviani,	♏x;
Vaselini albi,	℥j.—M.

Sig. External use.

Or,

℞. Unguenti hydrargyri,	ʒi–ij;
Unguenti aquæ rosæ,	ʒvj.—M.

Sig. External use.

Local fumigation, by exposing the parts, after softening with warm water, to the fumes arising from a few grains of calomel in process of sublimation, is often a valuable procedure. Bichloride lotions, such as the following, are serviceable and agreeable:

℞. Hydrargyri chloridi corrosivi,	gr. i–iv;
Glycerini,	f ʒj;
Tincturæ benzoini,	f ʒj;
Spiritus vini rectificati,	f ℥ss;
Spiritus rosmarini,	f ℥j;
Aquæ rosæ,	q. s. ad f ℥viij.—M.

Sig. External use.

Palmar and plantar lesions if persistent are best treated by inunction with mercurial ointment in 50 per cent. strength, or this may be combined with lanoline in varying proportions. This should be well rubbed into the lesions after softening the parts with warm water. If there is much scaling or thickening of the epidermis, shampooing of the surface with green soap may precede the inunction with profit. Or the following modification of the well known Lassar paste may be spread thickly over the part, and a light glove be drawn on to prevent its removal:

℞. Hydrargyri ammoniati,	gr. v–xxx;
Zinci oxidi,	
Talci,	*āā.* ʒij;
Vaselini,	℥ss.—M.

Sig. External use.

The tars and mercurials may be combined and used as in the following:

℞. Hydrargyri oxidi rubri,	gr. x–xx;
Olei rusci,	ʒj;
Vaselini,	℥j.—M.

Sig. External use.

℞. Unguenti hydrargyri nitratis,	ʒij;
Olei cadini,	ʒj;
Vaselini,	℥j.—M.

Sig. External use.

If the lesions do not yield readily, they may be touched once a week with a strong solution of acid nitrate of mercury or with pure nitric acid. Care should be taken not to permit too free action of the acid, as by such means much damage and pain may result. An alkaline solution should be at hand for use if needed. After severe stimulating treatment of this sort soothing applications, such as freshly prepared benzoinated zinc oxide ointment or the diachylon ointment of Hebra, should be used.

Moist papules, condylomata, and venereal warts occurring near the mucous outlets need to be frequently cleansed with warm borated lotions, and then to be dusted with calomel, boric acid, europhen, aristol, iodol, or iodoform. Bichloride lotions in the strength of 1:2000 or mild solutions of permanganate of potassium are valuable when used as a wash. Separation of the parts should be effected by pledgets of cotton and all possible sources of irritation should be removed.

Pustular lesions when appearing on the face should be opened and cleansed of their contents by the use of an antiseptic wash, after which each cavity may be filled with boric acid, europhen, or iodoform, and covered with a light dressing, such as a bit of surgeon's plaster. This can be removed readily and the dressing repeated as often as needed. Usually once in twenty-four hours is sufficient. In the case of gummata and tubercles, sponging with warm water and the application of mercurial ointment in full strength or reduced, as is thought best, is needed. A bit of mercurial plaster may be neatly spread over the part and allowed to remain. Care must be taken not to excite a dermatitis. If the gumma ulcerates, it must be cleansed each day of all crusts and accumulations of pus by washing with warm solutions of boric acid, and, after drying, the sides and floor should be brushed with a strong preparation of silver nitrate in distilled water, or the pencil of the same salt be used freely over all the parts. The cavity then may be filled with europhen, iodoform, or boric acid and covered with a snug-fitting but absorbent dressing. This is best accomplished by putting over the ulcer a layer of absorbent cotton or bichloride gauze and fastening it in place by adhesive straps or a neat-fitting bandage. On the face the dressing may be held in place by the use of flexible collodion. Pressure exerted upon the ulcer by drawing the edges together and holding them in place with rubber plaster often hastens repair. In the case of the lower limbs support of the parts by using the silk elastic stocking is decidedly serviceable.

Mixed treatment by the use of the iodides internally and mercury by inunction is called for in the treatment of these ulcers. The iodide should be given in drop doses of the saturated solution and pushed until the ulcer yields. Tonics are usually indicated.

When loss of hair begins the scalp should be shampooed every third night with the following:

R. Tincturæ saponis viridis,	f℥iij;
Spiritus lavandulæ,	fʒij.—M.

Sig. External use with warm water.

The head should be first bathed with water, warm as it can be comfortably borne, and then while still wet, a teaspoonful or more of the above should be rubbed thoroughly into all parts. The scalp is then washed clean with warm water and anointed with the following:

℞. Hydrargyri sulphidi rubri,	gr. j;
Sulphuris præcipitati,	ʒj;
Balsami Peruviani,	♏x;
Vaselini,	℥j.—M.

Sig. External use at night.

Or the following lotion may be used each night:

R. Hydrargyri chloridi corrosivi,	gr. ii–iv;
Tincturæ cantharidis,	f℥ss;
Spiritus vini rectificati,	f℥ij;
Olei amygdalæ dulcæ,	fʒij;
Spiritus rosmarini,	f℥j;
Aquæ rosæ,	q. s. ad f℥viij.—M.

Sig. External use on scalp.

The hair should be clipped close in the case of men in order to make the above-named preparations more easy of application.

In affections of the nails, where the nail substance only is attacked, the part may be shampooed each night with tincture of green soap, and after drying be thoroughly treated with an unguent made of equal parts of mercurial ointment and vaseline. If inflammation and ulceration take place in the tissues beneath and at the base of the nail, the finger or toe should be immersed in a warm solution of boric acid for ten or twenty minutes each day, and then dried and dusted with some suitable powder. The part should be protected by a linen cot.

Syphilitic lesions appearing in the mouth need the utmost care. All parts of the mouth should be kept scrupulously clean, and nothing should be allowed to pass the lips that can in any way irritate the lesions. Systemic treatment suitable for the condition should be pushed to the point of physiological toleration. Combinations of the iodides and mercurials are frequently needed. Locally silver nitrate in solution or by the pencil serves a useful purpose. Daily applications should be made. Gargles, such as the following, should be used at frequent intervals:

℞. Potassii chloratis, ʒj ;
Aquæ menthæ piperitæ, f℥viij.—M.
Sig. Gargle. Reduce with tepid water.

℞. Potassii chloratis, ʒj ;
Mellis despumati,
Tincturæ myrrhæ, āā. f℥j ;
Aquæ destillatæ, q. s. ad f℥viij.—M.
Sig. One part to four of tepid water, used frequently as a gargle.

Bellamy's iodized phenol may be used in the case of sluggish lesions with decided advantage. The following is the formula:

℞. Acidi carbolici, ʒj ;
Tincturæ iodi, fʒjss ;
Glycerini,
Spiritus vini rectificati, āā. fʒij ;
Aquæ destillatæ, q. s. ad f℥j.—M.
Sig. Ten to fifteen drops in a half tumblerful of water, used freely as a gargle.

A few grains of potassium chlorate or the five-grain tablets sold in the shops may be allowed to dissolve in the mouth several times during the day with decided advantage.

Gummata, owing to the rapidly destructive course they pursue, should be given prompt and energetic treatment. The iodides should be pushed as rapidly as possible to their physiological limit. Quinine in two-grain doses should be given four times a day. It is best to administer the drug in its powdered form, the local action of the alkaloid having a decidedly beneficial effect on the lesion. The pencil of silver nitrate should be used freely and the mouth washes and gargles continued.

Albolene sprays are useful in syphilitic affections of the pharynx and larynx :

℞. Acidi carbolici,	gr.j–ij ;
Olei caryophyllii,	♏iij ;
Menthol,	gr. ii–v ;
Albolene,	f℥j.—M.

Sig. Use twice a day with compressed-air atomizer.

Or,

℞. Extracti pinus canadensis destillati,	ʒss ;
Olei geranii,	♏iv ;
Albolene,	f℥j.—M.

Sig. Spray for throat.

Syphilitic affections of the nose refusing to yield to systemic treatment require fumigation with calomel or cinnabar. Stimulation with the pencil or a solution of silver nitrate is of value when the lesions can be reached. Inhalation of the following vapor is often of great service :

℞. Acidi carbolici,	ʒj ;
Tincturæ iodi,	fʒj ;
Aquæ ammoniæ,	fʒij ;
Spiritus odorati,	q. s. ad f℥j.—M.

Sig. Put in a wide-mouthed two-ounce bottle half filled with cotton. Inhale the vapor through the nose.

Ozæna should be treated by douches of mild potassium permanganate solutions or borated lotions. Thorough cleanliness of the parts must be maintained. Wiping the nasal passages with weak solutions of silver nitrate and then anointing them with ointment of the white precipitate or yellow oxide of mercury should be practised.

Affections of the bones call for the administration of the iodides in the fullest doses. In general it is well to combine mercury by inunction in the treatment. If the bone lesions are superficial, a small quantity of mercurial ointment, either pure or reduced with lanoline, may be gently rubbed into the part once a day, or a small piece of mercurial plaster may be applied to the skin covering the lesion, and kept in contact with it while it proves unirritating.

Gummata of the rectum and anus call for the iodides internally. Locally, thorough cleansing of all exposed lesions should be attended to each day, after which they should be stimulated with silver nitrate. The following ointment should be used before each stool by anointing the finger and passing it well up into the rectum :

℞. Tincturæ benzoini,	ʒj ;
Vaselini,	℥j.—M.

Sig. External use in rectum.

Stricture of the rectum needs to be treated by dilatation with rubber bougies or careful insertion of the finger tip. Rupture of the gut by too forcible expansion must be guarded against.

Syphilis of the epididymis and testicle needs vigorous treatment by the use of the iodides internally, and mercury by inunction. The mercurial ointment or a 5–10 per cent. oleate of mercury should be gently rubbed into the organ each night. The testicles need to be carried in a neat-fitting suspensory. Freedom from all sexual excitement must be insisted upon.

In syphilis of the heart mixed treatment is usually called for. It should be remembered also that strychnine, nux vomica, digitalis, and nitroglycerin can be used with as much advantage as in non-specific disease of the organ.

Syphilitic affections of the nervous system in general call for the administration of the iodides in increasing doses. It is well, however, in instituting treatment to begin with small doses of calomel, given at frequent intervals until the severity of the symptoms presented has been much reduced. A tenth of a grain may be given during the waking hours for the first three days, often with surprising benefit. The administration of the iodide may be interrupted at intervals while a short course of the mild chloride is being given, with good results. A combination of the iodides of sodium and potassium in equal parts is sometimes more efficient in its action than where either salt is given singly. Tonics and supportive measures are always needed. Stimulation of paralyzed muscles by the use of the faradic current must be resorted to at times in order to maintain nutrition of such organs. Daily rubbing of the body is often useful. Cool sponging of the entire body surface with salt and water, followed by brisk friction with the flesh-brush or a coarse towel, should be practised each morning. The feet should be kept warm and proper action of all the emunctories must be secured.

HEREDITARY SYPHILIS.

Syphilis is directly transmissible from the parent to the child as an inherited disease. The rôle played by either parent in such transmission is still, however, somewhat in question. Some syphilographers still hold to the belief that the child may inherit syphilis from the father while the mother remains sound and uninfected. That such paternal transmission can occur without infection of the mother seems extremely doubtful, and, if it ever happens, does so but rarely. The argument usually advanced in favor of the theory is that the mother never shows any signs of the disease. This, however, is hardly conclusive proof that she is unaffected. Colles' well known law affirms that a child suffering with inherited syphilis is incapable of infecting its mother at the breast, while the infant can infect any healthy wet-nurse in such manner. This law can be interpreted in but one way, and that is that the mother is suffering with the disease. Why it is that she manifests no symptoms no one as yet can tell, but the unquestionable fact remains that she is the possessor of the disease in a modified form, and as such possessor she can transmit it to her offspring. The universal acceptance accorded to this law by medical men is proof that its assertions are the statement of a recorded truth. Such being the case, the culpability of the father only in the process is seemingly disposed of.

The cases on record in which the mother, after having given birth to a syphilitic infant, has acquired a chancre and later developed true syphilis, are as rare as the cases of second acquisition of the disease, and it is highly probable that they can be accounted for in such manner.

If the mother remains uninfected, her child will undoubtedly escape. But if the mother be suffering from the disease, the probability is that her child will become infected also. Yet here the child may escape. The fact is undeniable that while both father and mother are still suffering with the disease they may at times produce children that never display any symptoms of syphilis. A syphilitic woman may produce a number of syphilitic fœtuses, then bring a healthy child into the world, and follow it in successive pregnancies with a number of children that are unmistakably suffering with the disease.

If the mother be infected during the course of her pregnancy before the termination of the seventh month, the chances are that her child will inherit the disease. After the seventh month the child usually escapes unless it be infected at birth by syphilitic lesions in the maternal passages. Such infection constitutes the acquired, and not the inherited, form of the disease, and is classed as *infantile syphilis.*

Abortion.—Few women suffering from active constitutional syphilis at the time of their conception carry its product to full term. Abortion is the rule, though exceptions to it may occur. In early stages of the mother's disease the fœtus is carried for a short time only. Usually the first product of conception after the development of constitutional syphilis is cast off before the expiration of the second or third month. Successive pregnancies are carried for longer and longer periods, until a viable child that may live for a few hours is brought into the world. Later the result is the production of a living child that may exhibit symptoms of syphilis before the expiration of the fourth month or remain entirely free from the disease throughout life. It is questionable if syphilis can remain latent throughout childhood and show itself for the first time at the puberal epoch. The probability is that in the cases apparently presenting such a condition the early symptoms of the disease were overlooked or misinterpreted. In the great majority of cases it can be asserted with safety that if the child inherits syphilis, unmistakable evidence of the disease will become apparent before the end of the first year.

SYMPTOMS OF INHERITED SYPHILIS.—A living child the subject of inherited syphilis may show no symptoms of the disease at the time of its birth. Usually, however, its features are drawn and pinched and the skin is wrinkled, giving to the infant's face the appearance of a "little old man or woman." The child does not grow, but remains puny and impoverished. The weazened look deepens and the skin assumes a sickly sallow hue. Characteristic lesions of syphilis may not appear for weeks or perhaps for months. When they are first announced they usually show themselves about the mucous outlets of the body, as the mouth and anus. Here they are displayed in the form of moist papules, mucous patches, and condylomata. Fissures show themselves within the mucous membrane at the angles of the mouth, while the skin bordering the part becomes the seat of similar lesions or of scaly reddened areas. Mucous patches develop in the mouth and throat, the tongue and inner border of the lips showing them oft varying numbers. The borders of the anus show moist papules, fissures, excoriations, and condylomata. The umbilicus may be affected in like manner. Coryza develops. Chief among the symptoms are snuffles. These are diagnostic of inherited syphilis. The discharge, at first thin and serous in nature, later grows profuse and becomes thick and mucilaginous. Swelling of the nasal membranes closes the passages. The process interferes greatly with nursing, and may wholly prevent it. The child experiences great difficulty in breathing. Extension of the inflammation from the nasal passages into the pharynx and larynx occurs, giving rise to a peculiar husky cry. Destruction of the bones of the nose may take place, with complete removal of that organ. Dry, scaling patches appear on the body, chiefly in the neighborhood of the buttocks. These dry patches are readily converted into moist lesions, owing to the warmth of the parts and the tenderness of the infant's skin. The condition changes from bad to worse. Nutrition is but feebly carried on, marasmus intervenes, and death closes the scene.

The above is the picture often seen in inherited syphilis. But in the inherited form of the disease, as in the acquired form, syphilis varies greatly in the manner and severity of its expression. Especially is this true if treatment be instituted early and carried on with vigor and under intelligent direction. The worst forms of the malady may be changed for the better and a great degree of improvement produced. It should be remembered that mercury is not contraindicated in a pregnant woman who is suffering with syphilis, and that in the administration of the drug exists the only measure that in any wise affords her a guarantee of producing a living child and of giving that child a chance to reach maturity.

If the malady is not to pursue the severe course outlined above, the symptoms of the disease are apt to be delayed. The child is well nourished at birth, increases in weight, and is plump and apparently healthy. Symptoms of syphilis usually become apparent before the end of the fourth month, but may not show themselves until somewhat later. They arise first, as in the severe form, about the mucous orifices, and are declared in the different varieties of moist lesions. Characteristic snuffles soon appear. An erythematous eruption of a part or the whole of the body surface may ensue. This rapidly becomes coppery in hue, and papules may develop. If unchecked, the skin lesions may take on any of the forms seen in acquired syphilis, and their subsequent behavior is in accord with the course that is there pursued. Dry papules arise upon the hands, feet, and face. Moist papules and condylomata appear about the anus and in all moist localities. Nodes, exostoses, and gummata develop within the bones, often resulting in great deformity of these structures. The brain, heart, lung, liver, eye, and testicle may become the seat of gummatous infiltration.

TREATMENT OF INHERITED SYPHILIS.—Treatment of a child liable to be the subject of inherited syphilis should begin while it is still in the womb of its mother. This is done by subjecting the mother to vigorous antisyphilitic measures. The sooner such a course is instituted after conception has taken place, and the more energetically it is pushed, the better will be the child's chances of coming into the world free from symptoms of the disease and remaining healthy afterward.

The plan of treatment best suited for mother and child under such conditions is that of mercurial inunction. This should be pushed at varying intervals to the point of producing distinct constitutional symptoms, care being taken not to cause actual salivation. With the first sign of systemic effects, such as the formation of a red line at the border of the gums, fœtor of the breath, or a marked metallic taste in the mouth, the inunction should be stopped and mixed treatment by the combined use of potassium iodide and biniodide of mercury be substituted. This latter course may be continued for from two weeks to one month as seems best to the judgment of the physician, when the inunction should again be resorted to. During this time hygienic and other measures calculated to improve the mother's health should not be neglected.

The mercurial preparations found useful in the internal treatment of syphilis can be employed, but not with the advantage to be obtained from the inunction. When used care must be exercised not to push their action sufficiently to bring on intestinal irritation and diarrhœa, as by such a course abortion may be brought about.

If the mother be suffering from late forms of the disease, such as gummata of bone, brain, or skin, potassium iodide should be given internally in full doses, while the inunction is being continued externally.

Lesions in the vagina, such as mucous patches and ulcers, need careful attention. The parts should be subjected each day to warm douches of boric acid or permanganate of potassium solution, extreme caution being used in not throwing the stream too forcibly against the uterine neck, as by such procedure premature labor may be excited. Frequent application by the physician of a solution of silver nitrate to the lesions is of decided value in promoting their resolution.

When the child is born with unmistakable symptoms of syphilis or develops such symptoms shortly after birth, its treatment must be begun at once. Great care, however, must be exercised by the physician in determining that the infant is actually suffering from syphilis. The offence is unpardonable on the part of the practitioner to pronounce every ailment of early childhood due to syphilis because the parents are suffering from the malady. Many children of parents who are the subjects of syphilis never show the slightest taint of the disease, and this is particularly apt to be the case when the mother has been given careful and energetic treatment.

Treatment of the child may be by the internal or external method as seems to the physician best suited to the case. External treatment should be by inunction, and is to be chosen in preference to the internal administration of mercurials when the tender skin of the infant can be made to tolerate the applications. This can be accomplished in most cases by exercising thorough care in the cleanliness of the child and by shifting, at frequent intervals, the places to which the ointment is being applied. Mercurial ointment may be used in the form of the officinal preparation or it may be combined with equal parts of pure vaseline or lanoline. Brodie's method furnishes decidedly the best means of applying the unguent. This is done by spreading the ointment freely upon the child's bellyband and keeping this in close contact with

..in. The part must be watched carefully, in order that a derma-
may not be excited. At the first appearance of redness the oint-
t must be applied to some other portion of the body. This can be
iy done by putting a band about one of the infant's limbs and spread-
this with the ointment, as in the case of the bellyband. In this
ner the inunction can be continued for quite long periods of time.
is often of great service to suspend the external treatment as occa-
n demands and resort to internal measures during the interval.

Where inunction is contraindicated or impossible, internal medication
y be instituted. Any of the mercurials used in the treatment of
hilis may be employed, but some, as calomel and the gray powder,
m productive of better results than others. Calomel is to be pre-
red in beginning the course, and, if it is found effectual in its action,
uld be continued. It ma n in doses varying from one twen-
th to one half of a grain nes a day. The calomel may be
nbined in powder form with sugar of milk, or one of the tablet trit-
ates supplied by all drug houses may be rubbed up fine and given in
little milk. It should always be administered after the child has been
d either at the breast or from the bottle. The gray powder may be
ven in the same manner as the calomel and in doses varying from one
nth to one grain. The bichloride can be tried when the above do not
nswer the purpose. It can be given in solution in doses of one two
ndredths to one fiftieth of a grain. A teaspoonful of this can be
ninistered in milk three or four times a day. The protiodide, binio-
ne, and black oxide may be tried in doses suited to the child's age, but
are not often well tolerated by the infant's stomach. The mercurial
given internally must be promptly stopped upon the appearance of
diarrhœa.

Tonics and cod-liver oil are frequently needed in the treatment of the infant. Iron may be given in the form of the citrate of iron and quinine, as follows :

℞. Ferri et quininæ citratis, ʒj ;
Syrupi aurantii florium,
Aquæ destillatæ, āā. f℥j.—M.
Sig. Three to five drops in milk twice a day.

Cod-liver oil is indicated when the child does not increase in weight, but remains puny and poorly nourished. The pure oil should be given. None of the much vaunted emulsions can be trusted not to disturb the stomach. The dose of oil should begin with ten drops, given best in milk, twice a day. This amount should be increased slowly as the little patient becomes tolerant of its action, until as much as a teaspoonful is being given two or three times a day.

When brain, bone, or visceral lesions arise, potassium iodide is indicated, and should be given three times a day in doses varying from one half to four grains each. The drug is extremely apt in these little sufferers to produce its peculiar acne and other forms of iodic rashes. Often the iodide can be given better combined with the biniodide of mercury, as indicated in the formula for mixed treatment (page 908) From three to ten drops of the mixture can be given in milk three times a day after the infant has taken food.

Local treatment of syphilitic lesions is indicated as in the adult, and the means described as useful in such cases can be employed here if modified to suit the tender condition of the infant's tissues. Mucous patches in and about the mouth should receive special care. The mouth should be kept thoroughly clean, and be treated freely each day with a mixture of honey and boric acid applied on a rag wrapped about the end of the finger. Snuffles should be treated by thoroughly cleansing the nose with warm boric acid solution, drying, and then painting the nasal passages lightly with a weak solution of silver nitrate. Afterward the parts may be sprayed with liquid albolene. A drop or two of Bellamy's iodized phenol in an ounce of albolene can be used with advantage in spraying the throat. The anal and umbilical regions should be kept scrupulously clean. If condylomata make their appearance in such places, they should be cleansed with warm water or boric acid solution, and then dusted thickly with calomel and talc in the proportion of 1 : 4.

The treatment of the mother should be continued in the form suited to her case. If possible, this should be by means of the mercurials, as potassium iodide is capable of suppressing the flow of milk. Such an accident is of serious import in the treatment of the child.

The child should always be nursed at its mother's breast, never at the breast of another woman. If for any reason the mother cannot supply the nourishment needed, the child may be fed on pasteurized cow's or goat's milk.

SYPHILIS AND MARRIAGE.

The length of time that must elapse between the date of infection and the time when marriage can be safely permitted depends entirely upon the course pursued by the disease. In some severe cases marriage ought never to be contracted. The number of such cases, however, is limited. In the majority of individuals infected in early life a time comes when it is safe for the patient, whether man or woman, to marry. For the individual who is sound and healthy at the time of infection, and who enters upon a thorough and effective course of treatment at once, following it faithfully for a period of two and a half or three years, marriage can be safely entered into between the third and fourth years. This, however, should not be done unless the disease has shown no manifestations during a period of at least six months, in which all medication has been suspended. In no case, no matter how slight may be the earlier symptoms, should the physician give his consent to marriage before two years from the time of infection, and this only when vigorous antisyphilitic measures have been followed during the greater part of that period.

The young man engaged to marry at the time of contracting the disease should be urged to make a frank statement of his condition to the woman in question, and to offer her a release from the agreement. She should be told fully the danger of her contracting the disease, even if she chooses to condone the fault and to continue the engagement, and the restrictions that will have to be placed upon her actions with reference to caresses and like approaches. Complete separation of the parties interested is advisable under such circumstances.

In the case of husband and wife the same frankness on the part
either should be required. Here, where the husband is so often
fault, a free, honest confession of his sin to his partner nearly alw
results in forgiveness and the continuance of the marriage bond. Se
ration by living at a distance from each other for a period of two
more years is the most desirable plan to be followed in such cases.
such a course cannot be pursued, cohabitation should be strictly forb
den and the occupying of separate beds be insisted upon.

LEPROSY.

By ISADORE DYER, M. D.

Synonyms.—Lepra; Elephantiasis Græcorum, Hebræorum; Leontiasis; Satyriasis; Ophiasis; Tzaraath (Hebr.); Kushta (Ind.); Juzam Dalfil (Arab.); Fa-Fung and Ta-ma-fung (Chin.); Boasi (So. Am.); Lebbra (Ital.); Radesyge, Spekalshed (Norweg.).

Definition.—Leprosy is an endemic, infectious, constitutional disease, due to a special bacillus, which in its development gives rise to structural changes of the skin and mucous membranes, nerves, bone, and other tissues, attended with general symptoms, anæsthesia, loss of tissue, and final deformity or death.

History and Distribution.—At the time of Christ leprosy was prevalent in the East. Before this era the history of leprosy is quite obscure. Indefinite references are made in the Bible in the books of Exodus (iv. 6); Leviticus (xiii. 24, 25, 43, 52); Numbers (i. and xii.), and Deuteronomy (xii.). It existed, probably confined in the early history of the world to Egypt and the Orient. In India the disease was recognized as early as fifteen hundred years before Christ. Six hundred years before Christ the Persians instituted measures to rid the country of the disease (Leloir). Celsus describes the condition in detail as early as the year 25 A. D. At this time Greece and Italy had been invaded. Galen in the second century chronicles the further spread of leprosy into Spain, France, and Germany. As early as 636 A. D. lazarettos were established in Italy. In the tenth century England and Scotland were afflicted. In the eleventh and twelfth centuries, during the Crusades, the disease spread all over Europe, reaching then the acme of its force and determining the subsequent measures for its control. At this time (at the death of Louis VIII., 1229) it was estimated that there were nineteen thousand leprosaries in Europe and two thousand in France alone.[1]

Yielding to this enforced control, the disease gradually disappeared from the fifteenth to the seventeenth century, surviving only in a few isolated districts.

With the disappearance of the disease in Europe it began in the colonies of the Americas and the islands of the Pacific and Indian oceans. No country or climate has been spared in the gradual distribution of the disease. It has spread wherever it has been introduced. Its appearance in a new country has always been directly traceable to importation from an affected country.

It is endemic in Northern and Eastern Africa, Madagascar, Arabia Persia, India, China and Japan, Russia, Norway and Sweden, I

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[1] Leloir, *Traité de la Lèpre*, Paris, 1885.

Greece, France, Spain, in the islands of the Indian and Pacific oceans. It is prevalent in Central and South America, Mexico, in the West Indies, the Hawaiian Islands, Australia, and New Zealand. It is found also in New Brunswick, Canada. In the United States the majority of cases occur in Louisiana and California, while from many other States cases are occasionally reported, notably from New York, Ohio, Pennsylvania, Minnesota, Missouri, the Carolinas, and Texas. In Louisiana leprosy has been gaining foothold since 1758, when it was introduced by the Acadians.

VARIETIES.—The varieties of leprosy usually described are three:

1. The tubercular;
2. The anæsthetic;
3. The mixed.

In the development of the bacilli of leprosy in the economy there are evolved neoplastic growths to which Leloir has given the name of "*lepromes*." These may occur at any part of the body and are responsible for the lesions of the disease. As they occur in the skin, in the mucous membranes, or in the nerves, muscles, bones, etc., so the affection is determined. For purely clinical reasons the disease attacking the skin and mucous membranes is given the name tubercular or cutaneous leprosy, while that attacking the nerves is called nerve leprosy, or the anæsthetic leprosy, or tropho-neurotic leprosy.

The mixed is the "complete" type sharing the physical characteristics of both of the above. Another variety is sometimes separated, the "macular." This may as well be called a type, as each is but a stage in the development of the entire disease, and it is indeed difficult to draw the fine lines necessary to the separation of the mixed from the merging anæsthetic and tubercular types. It is rare, moreover, to observe a case in which the pure tropho-neurotic or the pure tubercular type is maintained to the conclusion of the case.

ETIOLOGY.—The direct cause of leprosy is the *bacillus lepræ*; the indirect, contagion. This position needs some discussion, as the question of the contagiousness of leprosy is still an open one.

The contagiousness of leprosy is difficult of demonstration, because it is impossible to determine the period of incubation, and as yet no primary lesion has been discovered. Of all bacillary diseases, it alone is discriminated against by the anti-contagionists, and that with no positive argument. It is accepted as a bacillary disease and as infectious by many who will not admit contagion for lack of actual evidence. It resembles bacillary infectious diseases, especially tuberculosis and syphilis, in its methods of development. Further than this, there are evidences of contagion which cannot be combated—namely:

1. The undoubted spread of the disease. This is particularly notable in the Sandwich Islands and in Louisiana.

2. Its recrudescence after years of quiescence, even after apparent eradication, as in Brittany in France.

3. The history of individual cases of the disease in persons foreign to the region or climate who had contracted the disease when exposed, as Father Damien, Father Boglioli (Professor Jones's case in New Orleans), and numerous instances of nurses and attendants.

4. The accidental contagion, as in the medical student (reported by

Van Dyke Carter from Dr. Hatch's notes) in India who was accidentally cut while making a post-mortem on a leper.

5. Several members of the same family affected and successively with no history of ancestral leprosy. The author has 4 instances of this in point: 1, granddaughter and grandmother (Germans), the former affected two years before the latter; 2, two brothers (native Creoles), one affected several years before the other; 3, mother and daughter (negro Creoles), daughter affected seven years before the mother; 4, father and daughter (Irish), daughter affected seven years before the father. No history of exposure or of family tendencies in any of these cases.

6. The origin of the disease in single members of a family living in a leprous community.

7. The effect of isolation or segregation on the spread of the disease. (*Vide* Sandwich Islands in 1885, 4500 cases; Norway and Sweden in 1895, approximated 2500 cases; etc.)

8. The fact that neither age nor sex nor race is spared, while poverty and overcrowding and conditions of inferior hygiene seem to determine the selection of the lower social strata, as with many other infectious diseases.

9. Inoculation has been successful in one case (Arning), even if there may have been family predisposition.

10. Experiments with animals reproduce the disease *in loco*, if not systematically.

11. The bacillus is capable of culture on suitable soil (Byron *et al.*).

12. Leloir tabulates cases of direct infection between husband and wife in 17 cases, also tabulates cases of suggested infection from clothes and from the occupancy of houses formerly used by lepers (*op. cit.*).

13. The disease can be traced from one country to another.

14. The bacillus is found in leprous tissue and nowhere else. There are, besides, certain predisposing or general factors in the production of leprosy which must be considered. Chief among these is heredity. The fact that the disease occurs in successive generations and collaterally argues some force in heredity as a factor. Leprosy has never been proved hereditary or congenital, most cases occurring at ages precluding such an hypothesis.

The *Report of the British Leprosy Commission* in India, after the examination of 2000 cases (1893), concludes "*that leprosy in India cannot be considered an hereditary disease, and they would even venture to say that the evidence which exists is hardly sufficient to establish an inherited predisposition to the disease by the offspring of leprous patients to an appreciable degree.*" If the child is removed, leprosy is only rarely developed, and then it cannot be proven that there was no exposure to a possible infection (*ibid.*). In many so-called hereditary cases the child was affected first. A child often becomes leprous without family history and with no subsequent development in parents. The author has recorded 2 such cases: 1. A girl child of twelve with the disease two years; 2. A boy of six with the disease one year and a half. It is rare to see leprosy under the fifth or sixth year.

Individual predisposition is to be regarded among this class of general causes, as it must explain the exemption of one person while ano

ttacked. Among the contributing causes are the constitutional con-
ions, among which are syphilis, malaria, tuberculosis, scurvy, alcohol-
, and sexual immorality. Bad nutrition, bad hygiene, fish diet, espe-
lly in districts where half-raw fish is eaten, pork diet, changes of
perature, a moist climate, and vaccination (?) are further probable
ients in the production and propagation of this disease.

The majority of those affected are males, while the age ranges indefi-
ly from six to seventy-five, but cases are more numerous between the
s of thirty and fifty (Leloir and British Leprosy Commission).

PATHOLOGY.—The bacillus of leprosy in its development gives rise
ertain exudative changes, which begin ordinarily in the corium and
re associated with changes in the lymph vessels or the bloodvessels
emselves. The nerve lesions show a proliferation in the interstitial
nnective tissue. All (says Neisser) show a corre-
nding structure—a c d by sparse fibrillary interme-
te tissue. The cellular lymph corpuscles, gradually
ow in size until they are mes the original volume. The
lls are spheroidal, spindl unded.

The tumors in leprosy tissue, made up of cells which
row and form the "gia disease, finally breaking down
nd disappearing, leaving of connective tissue, fibrillary
character, most marked s where the nerve is affected.
ese cells are grouped a he bloodvessels, causing them
o hypertrophy and becom much thickened. Ultimately
he leprous tissue is absor nated, or it may be destroyed by
some ulceration brought al rnal factors.

The *bacillus lepræ* was disc 1868 by Hansen, but the descrip-
tion of it was not published until 1880,[1] and confirmed by Neisser in 1879.[2] Others to describe the bacillus were Cornil, Thoma, Hillairet, John Hillis, Köbner, Atkinson, Koch, Unna, and Thin.

The *bacillus lepræ* is described as a small rod bacillus, from one half to three quarters of the diameter of a red corpuscle in length, and in breadth about one fifth that length. It is straight or slightly curved, with pointed or rounded extremities. It occurs in short chains or beads resembling the tubercle bacilli (Byron), and may have its extremities clubshaped (Fig. 53, p. 925). The bacillus is readily stained with the anilines and by Gram's method.[3]

The bacilli are seen either contained within the "giant" cell or distributed in irregular groups in the granulation tissue.

The bacilli occur in all leprous tissues of the body. They are found in the secretions, with the exception of the urine. Köbner alone claims to have found them in the blood. Arning claims to have found the bacilli in the earth from a leper's grave (quoted in British Leprosy Commission). Various specimens of earth were examined by the British Leprosy Commission in India, and in several instances the germ was found. Various fish have been examined for the bacillus, but with negative results.

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[1] *Quart. Journ. Microscop. Science*, London, 1880, N. S. xx. 92-102; *Virchow's Arch.*, 1880, Bd. 79, p. 31.

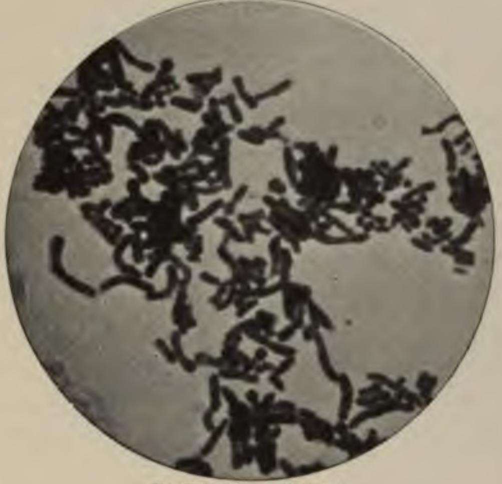
[2] *Breslauer Artzl. Zeitschrift*, 179, Nos. 20, 21; *Virchow's Archiv*, Bd. 84, p. 514.

[3] Sternberg, *Man. of Bacteriology*, 1892, New York.

Among others, Byron made a pure culture of the bacillus in agar-agar. This he has described in detail.[1]

In 1884, Arning inoculated Keanu, a Hawaiian, with leprosy, which was followed in six months by a well marked leprous tubercle at the site of the inoculation. Three years later Keanu had well marked leprosy. Discredit, however, is cast upon this experiment because the nephew, son, and maternal first cousin of Keanu were lepers.

FIG. 53.



Bacillus lepræ (Byron).

In animals Damsch, Campana, and Vossius have succeeded in reproducing the disease *in loco*, but not elsewhere. Melchior and Ortmann[2] succeeded in distributing the disease to the visceral organs, etc., following the introduction of a freshly extirpated leprous tubercle into the anterior chamber of a rabbit's eye.

SYMPTOMS.—All cases begin with the same preliminary manifestations, and it is only a small differentiation which determines the several stages. The incubation of leprosy is not definite. It is variously estimated at from a few weeks to twenty or even forty years, and the time is often wrongly reckoned from the possible exposure at a remote period, when it may have occurred far more recently. There are, however, certain prodromal manifestations which may determine the period of invasion. The one most constant symptom is the occurrence of fever, intermittent or irregular in periods and in type. Among the other notable symptoms are malaise, anorexia, dyspepsia, epistaxis, dryness of the nasal passages and respiratory tract, vertigo, headaches and neuralgias, rheumatic pains, articular pains, and exaggerated functions of the cutaneous fat and sweat glands. The latter especially is a notable symptom in developing leprosy, the sweating being almost periodical and associated rather with nervous than with febrile disturbances. There is in all instances a sense of anxiety, of anticipated calamity.

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[1] *Research. Loomis Lab.*, 1892, ii. 87–90.

[2] *Berlin. klin. Wochen.*, 1885, No. 13; 1886, No. 9.

There may be pruritus or hyperæsthesia of the skin, with neuralgic pains in all locations. These are the premonitory evidences of leprosy, often associated with indefinite eruptions of erythematous patches at various and irregularly selected parts of the body. Red at first, these spots become brownish, the borders white and occasionally thickened. These fade, and reappear in the same or other parts of the body, some fading, while others are making their appearance. Some persist for days, weeks, or months, finally fading, often quite rapidly.

This is the macular stage of leprosy, really only a group of symptoms of the premonitory stage. Now there may appear bullæ on the extremities, at the knees and elbows, wrists and ankles, but most often over the articulations of the phalanges of the fingers and toes. These may come in groups of bullæ, none larger than a split pea, or in single lesions the size of half a pigeon's egg, which appear as clear blisters filled with a yellowish white, semi-translucent fluid. Quickly, however, they become cloudy and pustular if they do not break through their thin walls. They heal quite rapidly, leaving behind a faint pigmentation or a superficial scar. Successive eruptions may recur for months or years before the determinate symptoms of confirmed leprosy appear. These may be characteristic at the start.

The tubercles may appear at once, and they vary in physical characteristics. They may be described as spherical or rounded nodosities, varying from the size of a pin's head to that of a hazelnut, hard and elastic to the touch, pale or red brown in color, at times copper colored, smooth, and telangiectatic.

In the negro these tumors are shiny and dusky brown, with a marked hue of red, the surrounding skin being much darker in color, especially immediately proximate to the periphery of the lesion. The lesions are discrete and form distinct individual nodosities, or they may become confluent, forming irregular oblong or gyrate bunched masses.

Often the eruption begins quite differently. The macules of the premonitory eruption may remain or other patches form, which vary in size, averaging the size of the palm. Usually simply hyperæmic or wine colored, they may be violaceous, livid, brown, yellow, or almost black. The centre is sometimes darker than the margin, sometimes depressed, free from color, an annulated lesion forming the patch.

1. *The Tubercular Type.*—In these patches the tubercles now form. There is a sudden rise of temperature, persisting irregularly. The patches thicken and grow elevated, become nodulated and bunched, forming irregular nodosities which gradually assume shape. They may remain under the skin, but more often grow until they are much enlarged and cause deformity by their prodigiousness. This constitutes the tubercular form of leprosy. The most frequent seats of the lesions are the face, the hands, the feet, the forearms, and the lower extremities. The face offers the favorite location for the eruption, and it is selective of the forehead, the eyelids, the nose, lips, chin, cheeks, and ears. The nose is flattened, infiltrated, hypertrophied, lobulated. The cheeks are likewise thickened, bunched, and nodulated. The ears become leathery, thickened, many times enlarged, and the lobules hang pendulous, often a mass of highly developed tubercles. The tubercles tend to confluence. They also tend to grow, and may become immensely hypertrophied,

exfoliate, or become complicated with œdema. Spontaneous retrogression may obtain. Then the lesions soften, sink into the skin, shrivel, and finally disappear, leaving a pigmented spot to mark the site. More often, however, the process is different. They become inflamed, suppurate, and slough in part or entirely. They may ulcerate in a superficial way, gradually destroying the subjacent tissues, attacking in turn the tendons, ligaments, and bones. On the mucous membranes the tubercles ulcerate readily, producing at first disturbances, then destruction of the affected region. Within the nasal cavity the septum gives way to the process, and early in the disease disfigurement results, with a consequent interference with speech and smell. Leprous deposits likewise form in the conjunctiva, gradually extend into the cornea, and affect the vision, finally causing ulceration and blindness. The glands are much enlarged in all regions, but particularly in the submaxillary and cervical.

The mental faculties are not much affected, excepting that there is a constant anxiety on the patient's part, anticipating some unknown and inapprehensible misfortune.

The testicles gradually atrophy, and, if the disease begins before puberty, the physical development is greatly retarded.[1]

Tubercular leprosy develops rapidly, and is liable to attack any region of the body. The destructive process attendant upon the ulcerating lesions, especially of the extremities, is more than likely to result in mutilation and deformity, in which this does not differ from the type presently to be described.

2. *The Anæsthetic Type.*—The anæsthetic or tropho-neurotic form of leprosy, or, as Leloir calls it, the "systematic nervous leprosy," differs in no respect from the tubercular in its period of invasion. The bullous eruption, however, usually appears as the single lesion, incessantly re-forming, until finally there is only an ulcer left, which becomes obstinate and persists with constant destruction of tissue. From this peripheral lesion anæsthetic or nerve leprosy may start. Beginning on one finger, the balance of the digits of the affected hand will one by one be attacked, followed by those of the hand on the other side. The feet may follow or present lesions at the same time. This is often the history. The ulcer becomes a trophic one, with a localization in the fleshy part of the heel, great toe, or the ball of the foot. It is painless and persistent. It is characterized by the sharply cut edges, the surrounding infiltrated and thickened skin, and the typical nauseous discharge.

The anæsthesia starting from these lesions extends up the hand and arm, associated with loss of sense of heat and cold, pain, and even touch at times. Then, or before, the macules of anæsthetic leprosy appear. The characteristic and most important lesion of this type is the macular patch, with a well defined pigmented, usually brown, periphery around an atrophic centre, free of color or of a parchment yellow hue. The edges are often thickened and elevated. The patches are often serpiginous or gyrate as a result of confluence. These patches are always markedly anæsthetic, the discolored parts being most anæsthetic and proportionate to the degree of color.

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[1] Neisser, in *v. Ziemssen's Cyclopædia.*

These are the lesions of the eruptive stage of the anæsthetic type, or Leloir's "period of invasion." The patches themselves may anomalously become hyperæsthetic, or points of hyperæsthesia develop at other parts of the body. Likewise, anæsthesia may occur without any determining lesions. Neuralgic pains are common, and marked thickening of certain nerves occurs, notably the ulnar.

Just here an almost constant symptom is evident. This is the anæsthesia of the little finger, which is present even before any lesions have appeared on the hand.

Following the eruptive stage is the permanent stage or the stage of degeneration. It is marked clinically by trophic disturbances, atrophies, paralyses, etc. Motor paralyses of the face, hands, and feet are soon evident. Insensibly the patient loses the power of grasping objects, the sense of touch, as well as loss of muscle control, being gone. There follows muscle atrophy of the face, distorting it, and of the hand, causing contractures. Ectropion of the lower lids results, so that the eyes cannot be closed. The lips become flabby and the lower one drops. The extensor and flexor muscles of the forearm contract, and the "claw-hand" results. The muscles of the lower extremities are affected in the same way. A shuffling gait, due to inability to raise the feet, and final incapacity of motion, result. Then come atrophy of the skin, shrinking of the skin, and a general appearance of senility. There are numerous trophic disturbances, such as falling of the hair, loss of pigment of the hair, loss of teeth, shedding of the nails, ulceration of the gums and of the nasal passages. The ulcers over the articulations of the phalanges extend to the articulation, cause the phalanges to fall, or, occurring in the middle phalanges, cause shortening or contraction. Dry gangrene, or necrosis, occurs; absorption of the bone and deformity result. The mutilating process may progress to the loss of the entire hand or foot.

3. *The Mixed Type.*—The "mixed" type of leprosy is, as its name suggests, a combination of the two varieties just described. It is the complete development of these two stages, with the symptoms and characteristics of each. It may begin with the anæsthetic macule and the prominent tubercle, both well defined and occurring simultaneously. More often one variety, usually the tubercular, assumes the type of the other. In this form of the disease the lesions are perhaps more prominent and the symptoms are more profound. Œdema of the extremities is quite common; the fingers lose their shape, become tense and shining, looking as if the skin would burst. The course and the result of mixed leprosy are the same as with the other stages.

DIAGNOSIS.—The diagnosis of leprosy can be made readily when the disease is well developed. Tubercular and anæsthetic leprosy can scarcely be differentiated until the lesions have matured. In the former the early bullous eruption is more often in groups; in the latter, in a single recurring lesion.

The following list contains the determining points in the diagnosis of all stages and types:

1. Habitat, whether community or family domicile;
2. History of contact with, or exposure to, the disease;
3. Anæsthesia;
4. Trophic disturbances;

5. Eruptions of bullæ in successive crops or of a single one recurring;
6. Perforating ulcers of the hands or the feet;
7. Muscle atrophy;
8. The "claw-hand;"
9. Clubbed fingers;
10. Discolored and blunted nails;
11. Characteristic anæsthesia of the little finger, an early sign;
12. The leonine face;
13. Leathery ears;
14. Ectropion of eyelids and lower lip;
15. Persistent mutilating ulcers at the articulations of phalanges of fingers and toes;
16. Deformity of fingers and toes from loss of phalanges;
17. Hunted, anxious look;
18. Loss of expression in the face;
19. Finding of lepra bacillus.

From *morphœa* the anæsthesia and color, with the absence of the areola, diagnose leprosy. *Syphilis* is diagnosed by the color, course in development, and the anæsthesia. *Iodism* is differentiated by the anæsthesia and absence of pustulation. *Sarcoma*, by the number of the lesions and the anæsthesia. *Molluscum fibrosum*, by the consistence, size, color, and duration of the lesions. *Lichen planus* is diagnosed by the color and absence of subjective symptoms; *pemphigus*, by the location and sequelæ of the bullous lesion. *Dysidrosis*, by the location of the lesions and the recurrence independent of season and of treatment.

Morvan's Disease.—If this is not regarded as a variety of leprosy, or if leprosy is not considered one of the causal elements, it is difficult of diagnosis, and only the finding of Hansen's bacillus will determine the differentiation.

PROGNOSIS.—The average duration of leprosy is about eight years. The mixed and the tubercular are the more rapidly concluded—in from four to twelve years unless shortened by some intercurrent disease. The spontaneous involution of lesions may be followed by no recurrences, but this is usually only a process in the final result, though the longevity of the individual may be increased by this remission.

Death is the ordinary conclusion of every case, which may come (in 38 per cent. of cases) from the exhaustive effects of the disease, from an almost necessary septicæmia, or from some intercurrent disease, as nephritis (in 22.5 per cent.); from pulmonary diseases, including phthisis (in 17 per cent.), diarrhœa (in 10 per cent.), anæmia (in 5 per cent.), remittent fever (in 5 per cent.), peritonitis (in 2.5 per cent.).[1]

TREATMENT.—The treatment of leprosy has been attempted according to almost every conceivable method, without marked results. The Pharmacopœia has been exhausted in the search for remedies having specific effect in the control and cure of the disease. The disease stares us yet in the face, unconquered and unabating.

The indications for treatment follow certain well defined lines. We must consider—(1) the tonic; (2) the palliative; (3) the specific; (4) the tentative; and, finally, (5) the prophylactic treatment of the disease. Recognizing leprosy as an as yet incurable disease, tonic treatment must e directed at maintaining the strength of the individual and at conributing as far as possible to the supply to meet the necessary waste. trychnine, arsenous acid, iron, quinine, cod-liver oil, hypophosphites, ang-nan, etc. are among the remedies suggested and used. Dietary d hygienic care must be included among the tonic measures employed. gular baths, cold or hot, vapor or medicated, are also included in this finition. It is well to adopt some one or more tonic remedies, and to persist in them throughout the treatment. The author insists upon the prolonged administration of strychnine sulphate or of arsenous acid. Palliative measures are employed for the symptoms which may arise n the course of any given case when ordinary judgment is required. Neuralgias, rheumatism, diarrhœas, or kidney disturbances must be reated appropriately.

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[1] Hillis' table, quoted by Niesser, *loc. cit.*

By specific treatment we mean the so-called cures and remedies dvanced as visibly and materially checking or removing the patent symptoms of the disease. The list of these is legion, but some of established value should be mentioned. Chaulmoogra oil, *Gynocardia odorata*, is perhaps the one remedy of this class for which most is claimed. It is used both externally and internally, but is best given in capsule or in milk. The dose varies from two drops to as much as the stomach of the patient will allow, and it is best given after eating.

Gurgun oil, *Dipterocarpus turbinatus*, is likewise used. It is usually given with lime water. Cashew-nut oil is still another of a large number of native oils employed in India.

Unna claims to have cured two cases with ichthyol internally, using ichthyol, pyrogallic acid, and resorcin externally.

Salol and salicylate of soda have attained a degree of favor recently, especially in the Hawaiian Islands. Goldschmidt of Madeira has used europhen by hypodermic injection into the nodules and patches, and claims results. The europhen was incorporated in oil. Tuberculin was used extensively in a tentative way at the time of its introduction, but with no appreciable benefit, and with some instances of decided harm. The author recalls one case in which death was materially hastened by its employment.

Since Carreau's monograph on the use of chlorate of potash in the treatment of leprosy I have employed this drug tentatively in several cases. The first case was enabled to take as much as 380 grains a day, with absolutely no intoxication from the drug; the quantity of urine was undiminished and the bowels were constipated. The drug was found in the urine, but there was no evidence of kidney disturbance. This treatment was carried on differently from Carreau's. He began with large doses, and increased them; I began with small doses, and increased them gradually to a tolerant point, being guided in this by the urine and the condition of the intestinal canal. In no instance was it necessary to stop under 180 grains a day, and in the instance quoted a maximum of 380 grains was reached. In this patient marked amelioration was produced, but only after a change of climate was made. He continued this line of treatment, however, and for a period of over six months averaged over two hundred grains of chlorate of potash a day.[1] Of 2 other cases, one responded for nearly six months, but relapsed into a worse condition than before, and the other died with acute parenchymatous nephritis. One case of cure (?) occurred, and is worthy of report:

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[1] Dr. J. C. Holliday's (Hot Springs, Ark.) notes of the case.

H—— G——, colored, tubercular type, aged fifty, born in Mississippi; lived since eighteen years old in Louisiana; worked several years in Mississippi on river boats, stopping at various points, some leprous centres; a cooper by trade. Was seen first on the 24th of February, 1893. At this visit a careful examination showed the following condition: A tall negro, probably six feet in height, African in type, rather under weight, fairly muscular generally. Presented lesions of marked type on face. In the interpalpebral space and on both cheeks were tubercles varying in size from a split pea to a hazelnut, telangiectatic, firm in consistency, shining, and each one anæsthetic. There were several macular lesions on the trunk. On the left arm there were three or four macular patches, not elevated, but infiltrated, well defined, however, against the surrounding skin. On the hand there were several small tubercles. There was already loss of sense of touch, with pain, in this hand. The hand could not be closed nor could any object be held for even a few moments. There was a paralysis of the muscles of the arm and forearm, and the patient had to be assisted in undressing for the examination. He complained of frequent paroxysmal "rheumatic" pains in the arm affected. No bacteriological examination was made, and no photograph could be had on account of the inclement weather. Ichthyol was prescribed internally in doses of 5 drops t. i. d., and also in 3 per cent. ointment; benzoinated lard was used for local inunction.

On March 3d the local application was changed to the officinal iodide of lead ointment.

March 28th. Since last visit the patient has had an eruption of bullæ on arm, some of which have left small ulcers. Advised oxide of zinc ointment to arm. Ichthyol continued.

April 4th. Arm improved. Stopped ichthyol and prescribed chlorate of potash, gr. xv, t. i. d., in sweetened water.

April 11th. Lesions on face smaller, better use of hands, arms better, lesion on arm healed. General sensation improved in hand. Bowels very loose; several actions daily, "almost white." Diuretic action marked. Pain in left ankle. Discontinued potassium chlorate. Bismuth subnitrate, gr. x, t. i. d., internally.

April 22d. Tubercles on face still smaller, flatter, and softer. Other lesions (macules) smaller and no longer anæsthetic. Resumed potassium chlorate (gr. xx, t. i. d.).

April 27th. Better, feels weak, anorexia, bowels loose. Discontinued chlorate of potash. Ordered—

℞. Tincturæ nucis vomicæ, ʒj;
Tincturæ cinchona compositæ, ℥jss;
Tincturæ gentianæ compositæ, q. s. ad ℥iij.—**M.**
Sig. Teaspoonful three times a day.

June 15th. Tubercles on face gone; slight pigmentation **rema** *in loco*. Ordered strychnine sulphate $\frac{1}{60}$ grain three **times** a

July 15th. No lesions anywhere visible; patient has complete use of hands. Has resumed his occupation. Feels well. Some anæsthesia of left arm and hand.

October, 1893. Patient reports for observation. No symptoms whatever of leprosy. No indication of former lesions beyond the pigmented spots in the site of the former tubercles on the face. (It is common among the negroes to find pigmentation following, often permanently, any inflammatory conditions.)

Carreau has emphasized the possible advantages in this drug, but in his two cases reported there were such violent toxic symptoms that he desisted. As early as 1800, Chisholm[1] reports the cure of one case with the *oxygenated muriate of potash*, administered in doses of 30 grains *per diem*, effected in "about six weeks." The accidental poisoning of a patient of Carreau's by a bite from a native venomous snake led him to use the drug, and he was apparently ignorant of its earlier usage, although Chisholm's field of observation was also in Jamaica.

It is a popular belief among the natives of South American countries that the bite from a venomous snake will result in the cure of leprosy. Carreau's observation[2] would give this legend some color, for in his case the nodules of confirmed tubercular leprosy disappeared as the victim recovered from the influence of the snake venom.

Winslow[3] gives a very graphic description of a fatal result in a case in which the patient subjected himself to the bite of a mature rattlesnake.

The recent experiments of Fraser[4] and of Calmette would place the possibility of experiment in this line within reach. The author believes that the investigation of the effect of "antevenene," or attenuated snake venom, upon the leprous subject might result in a new therapeutic measure for leprosy.

It is insisted, however, that the tonic treatment of leprosy must be constantly employed, even at the risk of depreciating the value of the latter experiments, as the patient is the first consideration. Within the past year Dr. Juan de Carrasquilla of Bogota, U. S. of Colombia. has published a report of several cases treated with serum derived from leprous lesions. From his report, marked improvement occurred in all types treated.[5]

Surgical procedures are often indicated in the course of the disease, but ordinarily these are met by the customary surgical judgment. Nerve stretching for the relief of the peripheral neuralgias or with a view of interrupting the leprous process is sometimes resorted to. Amputation of an extremity or digits affected is suggested, as giving a possible chance in aborting the disease.

Prophylaxis.—The prophylactic treatment is directed to two points: First, *individual isolation* in its strictest sense would preclude the possibility of spreading the disease. This, however, is scarcely practicable. Individual caution, then, is the next best measure. Here cleanliness, due protection of open lesions, the use of individual utensils in the household and of individual sleeping apartments, clothing, bedding, etc., with absolute prohibition of the family and social osculation and of the sexual relation, are the indications, though difficult to maintain.

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[1] *Edinburgh Med. and Surg. Journ.*, 1800, p. 399.

[2] *Observation au Traitement de la Lèpre*, Pte.-à-Pitre, Jamaica, 1892.

[3] *Lancet Clinic*, Cincinnati, 1874, vol. vi. p. 130.

[4] *Brit. Med. Journ.*, June, 1895.

[5] *New Orleans Med. and Surg. Journ.*, Nov., 1896.

Second, *Public Protection.*—There should be some protection offered the public. Moses promulgated stringent laws which today seem inhuman, while the popular horror of the disease has in no way abated. In this age of multiplying calamities, however, it needs more than a passing appeal to stimulate the public spirit to an active interest in a possible danger, apparently on the increase. Leprosy is a preventible disease, even though the question of infectiousness is still an open one. This prevention must come through State or national intervention. Where the control depends upon political State boards of health, with only a subsidiary idea of the demand and necessities of an exposed public, there must be conspicuous failure.

Norway and Sweden have settled the question by national legislation. The Sandwich Islands have likewise systematically improved their methods of controlling the disease. Louisiana for years has made abortive attempts at the control of the disease, and within a year has created a State board of control, with only restricted functions, and these further restricted by an apathetic public. California has not yet succeeded in this, exposed as she is to a constant source of infection from the Sandwich Islands, China, and Japan.

At best, State legislation only temporizes. As each State adopts laws for the segregation of the afflicted, these poor creatures only make matters worse by removing to a neighboring State which is without laws of either protection or extradition.

It is a vital and pregnant question for the National Congress to discuss and dispose of before the need becomes a crying one, and before the disease becomes so disseminated that a more than active effort will be required. The question of State rights, it is contended, would oppose national interference. It would only require the passage by each State of an act granting the national government requisition upon an alleged leper. More than this, State boards of health could be forced to remand recognized lepers to a national asylum. In this way systematic organized segregation would result, placed in the hands of those capable and empowered to care for, control, and investigate the disease.

TETANUS.

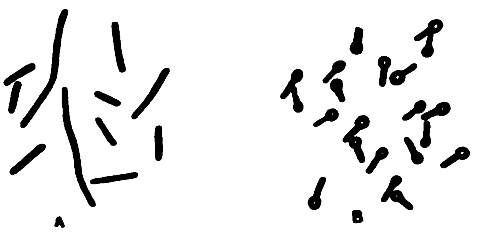
BY JAMES STEWART, M. D.

DEFINITION.—Tetanus is an acute infectious disease of the nervous system, characterized by persistent tonic spasm of certain muscles, with violent exacerbations.

ETIOLOGY.—Tetanus is due to infection by the tetanus bacillus. This bacillus was first discovered by Nicolaier of Göttingen in 1885 in garden earth. Kitasato in 1889 was the first to make a pure culture of it. It is a slender rod with rounded ends. It is only slightly motile. It develops best at the normal temperature of the body. Exposed to a temperature of 42° or 43° C., it quickly presents involution forms, and at a temperature of 60° C. it is promptly destroyed.

It is distinctly anaërobic, the presence of oxygen quickly destroying it. If protected from air and light, the spores in a culture remain virulent for more than a year. At a blood temperature in thirty hours, and at the temperature of an ordinary room after a week, spores develop.

FIG. 54.



Tetanus bacillus: *A*, vegetative stage, from gelatin culture; *B*, spore stage, showing pin shapes (Abbott).

The rods swell at one end, forming characteristic pinshaped bodies. The spore formation is devoid of motility. It is also much more resistant to the action of heat and antiseptic agents than the vegetative form, the former resisting the action of a 5 per cent. solution of carbolic acid for fifteen hours and 1.10 per cent. of corrosive sublimate for three hours.

Our present exact knowledge of the nature of the action of the tetanus poison has been derived chiefly from experimental work on mice and rabbits. The symptoms of tetanus in these animals are similar to those met with in man.

The period of incubation varies considerably, depending on the quantity and virulence of the poison and the susceptibility of the animal. In rabbits it is about the same as in the human subject, from eight to fourteen days, while in the mouse it is seldom longer than three days. The spasms appear in the lower animals first in those muscles [illegible] immediate neighborhood of the part which is the seat of [illegible] soon, however, spread and involve the entire muscular system. When the poison is injected into the veins or into the peritoneal cavity the spasms are at once of a general character.

In man the source of the tetanus poison can usually be discovered or rendered highly probable. It has been recognized for many years that wounds contracted in a certain manner were more liable to be followed by tetanus than others. For instance, wounds inflicted with splinters of wood, old rusty nails, and those contaminated with earth or with the excrement of horses were known to be especially dangerous in this respect. This knowledge was common long before the discovery of the tetanus bacillus, and before even it was considered possible for tetanus to be due to a living outside poison. The tetanus bacillus and spores have been frequently demonstrated in garden earth and in all kinds of earthy matter, in the dust [illegible] houses, in splinters from the flooring, walls, and windows [illegible] in fact, the poison may be said to be so abundant that one m[illegible] surprised how comparatively rarely the disease is met with. [illegible] explainable when we recollect that the bacillus is quickly destroyed [illegible] exposure to oxygen, a few hours' exposure being sufficient to [illegible] its toxic properties. It therefore [illegible] rarely develops except in deep, penetrating wounds. Tetanus, so far as is known, is only developed from the introduction of the poison into a wound. Experimentally it cannot be induced in the lower animals through the stomach or respiratory tract. As far as known, the same is true of man. To account for cases of what was formerly known as idiopathic tetanus it is necessary to assume some slight lesion of the surface in some part which has escaped notice. It now and then happens that the tetanus poison is introduced alone, and in such a case a trifling abrasion may heal by first intention. As the tetanus bacillus has no pyogenic properties, no pus or other discharge will be present. In the present state of our knowledge we must con[illegible] that the poison of tetanus is always introduced through an actual lesion of the skin or mucous membrane, the lesion in some cases being so trifling that it may have healed completely before the symptoms of the disease have developed.

It has been clearly proven that the symptoms of tetanus are not brought about by the bacillus directly, but through the action of a toxin generated by it at the seat of the wound. The filtrate of a tetanus bouillon culture which is perfectly free from the bacillus can induce the same symptoms as the injection of the bacillus itself: this shows that the poison exists as some chemical substance separable from the bacillus.

A filtrate made from a tetanus culture of four weeks' growth placed in [illegible] alkaline grape-sugar bouillon contains the poison or poisons in [illegible] active state, a quantity not exceeding the 0.000005 c.cm. of this filtrate being sufficient to kill a white mouse. If kept in a cool place and protected from the light, the filtrate retains its poisonous properties unchanged for many months. Brieger has obtained two substances from such filtrate, to which he has given the names of *tetanin* and [illegible], each of which he found were capable of causing death in animals with all the symptoms of tetanus; but very large quantities of both were necessary to induce the symptoms of tetanus; hence it is to be concluded that neither of these bodies is the active chemical agent, seeing that the very smallest quantity of the filtrate is sufficient to induce a fatal result.

Brieger and Fränkel have obtained a *toxalbumin* through precipitation with alcohol, which they found much more active than the basic bodies discovered by the former. Even this toxalbumin is much less poisonous than the filtrate itself. Further experiments in this direction have not as yet led to any definite knowledge as to the composition of this remarkable poison. It probably is not an albuminous body, as it develops readily in matter free from albumin.

Tetanus occurs at all periods of life. It is met with in newly-born children (tetanus neonatorum) and in advanced life. It is more frequent in males, on account, no doubt, of their greater exposure to the exciting causes. It is considered to be more frequent in the dark-skinned than white people, even in the same country. It has long been recognized that it is much more frequent in hot than in cold countries. In the East Indies, Central America, and the West Indies it is much more common than in Europe or North America.

The development of the tetanus bacillus is favored by its being introduced in company with other bacilli, especially those having pyogenetic properties (streptococci, staphylococci, etc.). It was formerly taught that cold was an exciting cause of the so-called idiopathic form, but in the light of recent researches this idea must be given up. The not infrequent appearance of tetanus in soldiers wounded in battles can be more readily explained by the contamination of the wounds with earth than by supposing that cold is an active agent.

In all probability mental anxiety, alcoholism, and other debilitating causes have a more or less predisposing influence, as they lessen the resisting power of the tissues in general.

Puerperal tetanus, a not uncommon variety in hot countries, but extremely rare in temperate climates, is one of the most serious forms in which the disease is met with. It occurs after abortion, and also after labor at or near the full time. It generally occurs where there has been some complication, either during or after the expulsion, hemorrhage, conditions requiring the use of the forceps, adhesion of the placenta being the most frequent. It is not necessary to assume that in puerperal tetanus there is any special cause or factor at work other than the bacillus.

Tetanus neonatorum, like the puerperal variety, is a disease essentially of tropical countries. There is, however, one striking exception to this rule: in the island of Heimacy, near Iceland, the population at one time was kept up only by immigration, almost all the children dying from tetanus.[1]

The infection in tetanus neonatorum occurs through the umbilical wound. Tetanus occurs also after the operation of circumcision in hot countries.

PATHOLOGICAL ANATOMY.—In a few cases of tetanus slight changes have been found in the central nervous system. It is, however, extremely doubtful whether they have any significance, being probably the result of the fever and convulsions directly, rather than the effects

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[1] Gowers' *Diseases of Nervous System*, vol. ii. p. 679.

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The rigidity of the different muscles is an almost constant condition during the progress of the disease, varying, however, from hour to hour. It often ceases during sleep, whether brought about spontaneously or artificially (chloral, opium, chloroform). The muscles, however, at once assume their rigid state when the patient awakes.

In addition to the constant rigidity, in nearly all severe cases are sudden exacerbations, coming on with great suddenness and lasting from a few seconds to two or three minutes. The previous muscular distortions are greatly intensified. The contractions of the features are frightful to behold. The face and extremities become livid. The tongue may be caught between the teeth. These intermittent paroxysms may arise spontaneously or from some outside irritation, such as a draught of cold air, the least touch, or a voluntary effort. The suffering of the patient is agonizing in the extreme. During all this suffering the mind remains clear.

The temperature varies much in different cases. Frequently it has been found normal throughout the entire course of the disease. As a rule, there is a moderate pyrexia, from 101° to 102° F. In fatal cases the temperature, if not elevated in the earlier stages, generally rises to 103° or 104° F. before death. In those cases where pyrexia is present throughout it is usually found that there is no morning fall or evening rise. Sometimes a slight rise during the period of exacerbation has been noticed. Again, very sudden and very irregular changes occur in the course of the pyrexia. Hyperpyrexia is not infrequent in the fatal cases, the temperature rising for some time after death. Temperatures of 110°, 111°, 112°, 113°, and even 114° F., have been recorded.

The cause of the pyrexia is not fully established. No doubt the excessive muscular work is an important factor. The writer has met with hyperpyrexia in a fatal case of strychnine-poisoning. One hour before death the temperature was found to be 108°, and in half an hour it had reached 109° F. The same cause being at work in tetanus—muscular overaction—will account for some cases. It, however, must be remembered that in pontine and cervical cord lesions hyperpyrexia is a fairly common symptom.

The pulse is slightly quickened, especially during the acme of the paroxysms. It is often small (vasomotor spasm). In fatal cases it becomes very weak and rapid, 160 to 200 in the minute.

In severe cases the skin is bathed with perspiration. The urine is usually scanty and high colored. The amount of nitrogen excreted is said not to be increased, even when pyrexia is present. The patient may be unable to pass urine, owing to the spasms of the abdominal muscles. Obstinate constipation from this cause is the rule.

Cephalic Tetanus or Hydrophobic Tetanus.—Under this heading it is necessary to describe a rare variety of tetanus which was first observed by Rose. It results from wounds in the region inner
by the cranial nerves, especially the fifth. The special featur
variety is that the trismus is associated with paralysis of
the same side as the injury. Usually there is also mar
the pharynx and œsophagus, hence the term hydrophobi
addition to the paralysis of the seventh nerve, paraly
and fourth nerves has been met with.

The paralysis of the facial has the distribution of a peripheral palsy, but it is not attended with any changes in the electrical reactions. In the few cases examined after death no inflammatory or degenerative changes have been found in the nerve. These facts, together with the observation that in some cases the paralysis has disappeared after a few days, while the tetanus symptoms have steadily progressed to a fatal ending, lend strong support to the view that it is brought about in a reflex manner, and is not due to any coarse lesions in the nerve trunk.

Cephalic tetanus runs, as a rule, a feverless course.

COURSE OF TETANUS.—The duration of the disease is very variable. In very rare cases a slight but temporary rigidity of the muscles of the neck and jaw is the only manifestation of the poison. Cases presenting such a course have been called abortive forms. It is more than doubtful whether it can be fully established that such cases are really tetanus.

In very severe cases death may take place within two or three days or even in a shorter period. The duration in a fatal case is, however, usually from eight to twelve days. In the cases that recover the disease ends very gradually, the intermittent spasms disappearing, and then more slowly the persistent rigidity ceases.

Recovery is usually complete in from three to six weeks. In the case already alluded to of accidental inoculation with a tetanus filtrate the symptoms had all disappeared on the forty-first day in the same order in which they appeared. True relapses are unknown in tetanus.

Death may be brought about in various ways. In the acutest cases it is usually produced through spasm of the respiratory muscles, death being due to asphyxia through the arrest of respiration. Sudden death may also arise from cardiac failure during a paroxysm.

Death may be slow, due to gradual exhaustion. Cases are reported where the patient succumbed from exhaustion even after all spasm had ceased.

DIAGNOSIS.—During the first few days there may be uncertainty as to the nature of the disease. The stiffness of the neck may be mistaken for rheumatism, but it is soon followed by the trismus, which clearly points to tetanus. In trismus from dental irritation, tonsillitis, or inflammation of the temporo-maxillary joint there can be no difficulty in making a differential diagnosis.

The characters of the developed disease may be simulated by strychnine-poisoning, hydrophobia, hysteria, and tetany. In strychnine-poisoning the onset is sudden, the spasm being general. In tetanus the onset is slow and progressive, the spasms beginning in the jaws and neck and involving the trunk muscles after some hours or even days. In strychnine-poisoning the muscles of the extremities are more affected than those of the trunk; the contrary is the case in tetanus, the upper extremities being very rarely the seat of spasm. The reflex excitability in strychnine-poisoning occurs early, while it is a late event in tetanus. In the former death or recovery takes place in a few hours, while in the latter it is usually a question of many days. The differences are so striking that ordinary care in examination should prevent a mistake.

In hydrophobia the first symptoms are attacks of difficulty of breathing from attempts to swallow. There is no rigidity of any of the muscles in the early stages of the disease. In the later stages the tetanoid attacks do not resemble those of tetanus. The difference in the incubation period and the previous history afford in themselves sufficient evidence, in the great majority of cases, to clearly differentiate between the two diseases.

Trismus lasting a few hours or days is sometimes met with in hysteria, but it is not accompanied with the other symptoms of tetanus. If there is general tonic spasm, it alternates with general convulsions. Its onset is sudden, as is also its disappearance. Further, there will be a history of similar previous attacks, together with the stigmata of hysteria.

The positions of the hands and arms in tetany are sufficiently characteristic to prevent any mistake being made in diagnosis.

PROGNOSIS.—In all the different types of tetanus the mortality is very high. It is greatest in the puerperal type, extremely few cases recovering. It is said that recovery is almost unknown in tetanus after abortion. In the other varieties it ranges between 45 and 90 per cent., as a rule being nearer the latter than the former figure. The severer the injury the graver the prognosis. Tetanus following lacerated wounds or compound comminuted fractures is more serious than that following slight wounds. In suppurating wounds the danger is greater than in those that heal by first intention. The sooner the symptoms supervene after the infliction of the wound (infection), the greater the danger. Probably not more than 3 or 4 per cent. of cases recover where the symptoms arise before the end of the tenth day. If the incubation period is from two to three weeks or more in duration, then the chances of recovery are much greater (25 to 50 per cent.).

Exposure to cold at the time of infection lessens the chances of recovery. Unfavorable symptoms are early general muscular rigidity, difficulty in swallowing, and considerable pyrexia. In tetanus neonatorum the prognosis is the better the longer the interval after birth.

TREATMENT.—*Preventive.*—In all cases of wounds contaminated with earth, manure, etc. it should be a rule to make a thorough bacteriological examination for tetanus bacilli. Splinters of wood, etc. removed from wounds should also be examined with the same end in view. If such procedures were common practice, there can be no doubt that in some cases tetanus might be prevented. If some of the suspected material is injected under the skin of a mouse, and if the animal dies in two or three days with the symptoms of tetanus, it should be sufficient warning to make a most thorough disinfection of the wound and place the patient on the special serum treatment which will be presently fully referred to.

It is here unnecessary to dwell on the importance of thorough cleansing of wounds, no matter how simple they may appear at the time. In deep-seated wounds this precaution is especially necessary, as it is in this class of injuries that the tetanus bacillus finds the appropriate conditions for its development. If it has been demonstrated that the secretions of a wound contain the tetanus bacillus, then it may be a justifiable practice to excise the infiltrated parts, or even to amputate if the wound is situated on an extremity. If the symptoms of the disease have set in, experience shows that nothing is gained by either cauterization, excision, or amputation. In the uncommon cases where the symptoms first develop in the immediate neighborhood of the wound it would be sound practice to remove a portion of the peripheral nerve leading to the wound area. Several cases are on record where this procedure has been successful in preventing the further development of the disease.

TREATMENT.—The treatment of the developed disease will be considered under the following heads:

1. By antitoxin serum;
2. Ordinary medicinal agents;
3. General management.

The Antitoxin Serum Treatment.—It has been clearly shown by Kitasato, Behring, Roux, and Vaillard that the blood serum of animals rendered immune to the tetanus poison has marked therapeutic powers. Kitasato and Behring first showed that it was possible to confer complete immunity against the tetanus poison, even in animals the most susceptible to it. Mice, rabbits, and horses are very susceptible to tetanus. Behring's method of conferring immunity in these animals consists in injecting a bouillon culture weakened with trichloride of iodine at intervals of three to eight days. On the first day the bouillon culture is diluted with 0.25 per cent. of the trichloride; on the second day, with 0.20 per cent.; on the third day, with 0.15 per cent.; and on the fourth day, with the undiluted culture. The injections are continued at intervals in gradually increasing doses until complete immunity is obtained.

The blood serum of an animal rendered immune after the above method is capable when injected into another animal of conferring immunity to the action of the tetanus poison. It has been proved by Behring that mice when injected with a certainly fatal dose of tetanus poison can be saved by the use of the immunizing serum, provided this has been effected within five hours of the first appearance of the symptoms of tetanus. If twelve hours have elapsed before the serum has been injected, then it has been found to have no controlling influence. He also demonstrated that the injection of the immune serum a quarter of an hour after the injection of the tetanus poison had much less effect than when used immediately before. He found that it required a serum a hundred times more potent to have the same effect when injected a quarter of an hour after as when used before the introduction of the poison.

As to the results of the antitoxic serum in the tetanus of man, experience up to the present has not been sufficiently extensive to fully demonstrate its usefulness. A number of cases have been recorded where it apparently proved effective in saving life, but as a certain number of cases recover under all forms of treatment, it would be premature to assign to the serum treatment a directly antidotal action. Practically, a very great difficulty is met with in the treatment of tetanus by this method; that is, the disease is fully established before the treatment is resorted to. From Behring's experiments on animals referred to above it is clear that the immune serum is only effective when it is administered very soon after the first appearance of the symptoms. There is every reason to believe that the same holds good in the human subject, and that to be effective it should be used early (within a few hours).

It has been questioned whether the antitoxic serum acts on the same tissues as the tetanus poison. The action of the latter is chiefly on the central nervous system when the disease is fully established, while it is contended that the serum has no direct influence on these tissues. If these contentions were true, it would fully explain why the results are so slight once the disease is fully established.

In carrying out the treatment of tetanus with antitoxin Tizzoni-Cattani's preparation has been chiefly employed, for the reason that it is a much more stabile compound than others. It is an aseptic serum in a desiccated state. It can be kept for an indefinite length of time when protected from moisture, while the other tetanic antitoxins generally undergo decomposition.

The desiccated powder, according to Merck, is to be dissolved in distilled water in the proportion of ten parts by weight to one of the desiccated serum. All the appliances used in making the solution should be thoroughly disinfected by heat, but allowed to cool previous to bringing them into contact with the antitoxin, as the latter decomposes at high temperatures. As imported from Italy by Merck, the desiccated serum is in small bottles, and it is recommended to inject the contents of half a bottle for a first dose, while the remainder is divided into four equal quantities and injected at intervals depending on the result of the first dose and the symptoms of the disease. If the incubation period has been very short and the symptoms pronounced, indicating a severe infection, it is recommended to inject the contents of one bottle for a first dose, and to follow this by further injections, the length of the intervals to be governed by the action of the first. In children one half the adult dose is considered to be sufficient.

Tetanic antitoxin is considered to be free from danger. As prepared by Tizzoni and Cattani it is obtained from the blood of horses and dogs. "Its power of rendering immune is ascertained on rabbits—viz. on the basis of infectious or tetanic intoxications, which kill control animals in four or five days. The quantity of dry serum contained in each bottle is inversely proportionate to its power of rendering immune, and always considerably larger than that which, according to the experiments on animals, would have to be considered as the minimum curative dose for man" (Merck).

As already mentioned, sufficient evidence is not as yet at hand to enable us to give a decided opinion as to the value of antitoxic serum. There is a general consensus of opinion, chiefly founded on experimental work in small animals, that it has a very powerful prophylactic action. We further believe that there is more or less proof that it is also effective in cases in man where it has been used early and where the tetanus runs a subacute or chronic course. It has been used in a considerable number of cases, but rarely alone, other agents being also employed. It is difficult on this account to determine what effect it has had. In cases that run a very acute and severe course its action has been slight, if not *nil*. From this it would appear as if it had no counteracting influence on the poison already absorbed, but from its action in animals it is clear that it has great power in preventing the development of the poison. It should therefore be resorted to whenever there is the least symptom suggesting the possibility of tetanus.

The Treatment of Tetanus by Ordinary Medicinal Agents.—Among the remedies usually recommended in tetanus the following may be mentioned: chloral, opium, the bromides, Calabar bean, curare, carbolic acid, Indian hemp, chloroform, atropine, etc.

Cases are recorded where recovery has followed the employment of each of the different agents mentioned. Of no drug can it be said that it has a marked effect for good in severe cases, and, as recovery follows all possible modes of treatment in mild attacks, it is natural to conclude that the drug treatment of tetanus is far from satisfactory.

Of all agents employed, chloral hydrate is probably the most efficient. It should be given in large doses—from one to two drachms in the twenty-four hours. Many cases of recovery from tetanus are on record where chloral and morphia have been given in combination, and also where chloral and bromide of potassium have been given.

Calabar bean and its alkaloid, physostigmine, have apparently been successful in preventing death in a number of cases. The dose of the officinal extract is about one sixth of a grain. It should be given hourly until the physiological effects of the drug are induced. There is great tolerance of this as well as most other motor depressants in tetanus. The salicylate of physostigmine may be employed instead of the officinal extract of the crude drug in doses of one twentieth of a grain every hour or two.

Curarine, the active principle of curare, can be employed in doses of one two-hundredth of a grain. It should be given hypodermically, as it possesses but little action as a depressant on the motor end apparatus when given by the stomach.

General Management.—The patient should be kept perfectly quiet in a dark room. Visitors should be absolutely excluded. The diet should be liquid, and if the trismus is so marked as to prevent the patient from opening the jaws, he should be fed by the rectum, or by the stomach by means of a long tube passed through the nose. The practice of giving chloroform to relax the trismus in order to feed the patient is hardly to be commended, as its action is very frequently followed by an increased intensity in the tonic spasm.

If death is immediately threatened by spasm of the respiratory muscles, chloroform may be administered or artificial respiration performed.

INFECTIOUS FEVERS OF OBSCURE NATURE.

BY WALTER B. JAMES, M.D.

A CERTAIN number of cases of febrile disease are met with whose clinical histories suggest that they are infectious, but whose classification has not yet been perfectly established.

The existence of these as individual diseases is doubted by many observers, and, indeed, of no one of them can it be said that its right to a permanent place in medical classification has been demonstrated. Yet it seems wise to give some place to a discussion of them in a treatise such as the present one, more with a view to the encouragement of a systematic effort to clear up their obscure features than with the idea of dogmatically establishing their individual existence.

WEIL'S DISEASE.

DEFINITION.—A disease which is apparently infectious and which is characterized by fever, intense prostration, jaundice, and disturbance of the gastro-intestinal functions.

Attention was first called to this disorder by Weil in 1886. He described it as it occurred in a limited epidemic. Many cases have since then been reported in Europe and a few in America. It is sometimes called "acute infectious icterus."

ETIOLOGY.—Regarding its etiology we have no definite knowledge, but the behavior of the disease indicates that it is probably an infection. Of the nature of the poison we know nothing, nor of its source and mode of entrance into the body. It has occurred in a number of instances in limited epidemics in prisons, workhouses, and barracks, thus suggesting that crowding and unsanitary surroundings are factors in its production. Jaeger claims that it is due to infection with a proteus, the bacillus *proteus fluorescens*. The relation of the disease to simple catarrhal jaundice is interesting. Some have claimed that the cases described as Weil's disease are really only gastro-duodenitis with pronounced constitutional symptoms. Others believe that a large number of the cases generally described as catarrhal jaundice are examples of Weil's disease. In the cases hitherto reported there is a uniformity in symptoms and a general resemblance to the infectious diseases that make it seem best to classify it as a distinct disease under the above title.

PATHOLOGICAL ANATOMY.—In the autopsies that have been made there have been found only the lesions that are common to all the infectious fevers. Acute degeneration of the liver and kidney is generally present. Bacteriological examinations have yielded no positive result.

SYMPTOMS.—Weil's disease attacks men rather more often than women, and is most prevalent in the summer months. There is generally no prodromal period, the disease beginning suddenly. It is in many cases ushered in by a chill. The temperature rises rapidly and early reaches its highest point. Sometimes on the fourth or fifth day there is a remission of the fever, but after an interval of two or three days it recurs. The fever lasts from eight to ten days, and disappears gradually, without a well marked crisis. In some cases, after an interval of from one to eight days, there is a distinct relapse, the fever returning and lasting a variable number of days, subsiding again gradually. The pulse is rapid and full, later on becoming slower when the jaundice is well marked. Generally, from the very beginning, there is intense prostration, which is often the patient's chief complaint. There is some mental dulness and apathy. There may be delirium and coma. There may be intense muscle pains, generally in the back of the neck and in the legs. These occur in about 50 per cent. of the cases. Gastric symptoms are generally present and occur early. The tongue is coated and may be dry. There is vomiting. There may be either constipation or diarrhœa.

There is enlargement of the liver in about 50 per cent. of the cases, and the organ is tender to pressure. The spleen is enlarged in 75 per cent., and this occurs early in the disease.

Jaundice is always present, and commonly comes on early, though it may appear first when the temperature and other symptoms are subsiding. It varies much in intensity in different cases, and is believed to be due to biliary obstruction.

The urine is diminished in amount, contains bile pigment, and in more than 50 per cent. of cases contains albumin and hyaline and granular casts. There is sometimes hæmaturia.

COMPLICATIONS AND SEQUELÆ.—The complications and sequelæ are those common to the infectious fevers in general. In some cases there is a more or less severe catarrhal inflammation of the throat. Sometimes there occurs during the disease a purpuric eruption. The itching which belongs to the jaundice may be severe. In some cases parotiditis has been present.

DIAGNOSIS.—The disease is most apt to be mistaken for typhoid fever with jaundice, and for simple catarrhal jaundice. From the former it is to be distinguished by its sudden onset with the absence of prodromata, by the characteristic remissions, the absence of the eruption, and by the shortness of its course. From the latter the differential diagnosis is difficult, and in many cases impossible.

PROGNOSIS.—The prognosis is generally good, though a few deaths have occurred.

TREATMENT.—In the early stages calomel may be given in small doses, or castor oil. The use of violent purgatives should be avoided. Alkaline mineral waters, such as Carlsbad, are often used. Irrigation of the large intestine with cold water is sometimes of service. The diet should be of milk.

MALTA FEVER.

SYNONYMS.—Rock fever; Mediterranean fever; Neapolitan fever.

ETIOLOGY.—Malta fever occurs with greatest frequency on the island of Malta. It has also been met with in various Mediterranean ports, especially Naples. It is supposed to be identical with a local fever that has been observed at Cyprus and in some of the Red Sea ports. It has never been described as occurring in the Western Hemisphere. In Malta it develops with greatest frequency during the hot season. It attacks large numbers of the garrison, also many sailors in ships at anchor in the harbor. It shows no predilection of age or sex, but selects by preference newcomers to the island.

Regarding the nature of the disease we are uncertain. It is possible that it is a modified form of typhoid fever, but many observers who have studied it believe that it is a specific fever with a definite poison of its own.

The infection of the disease is apparently conveyed through the air. There is no evidence that it is communicated by food or drinking water.

PATHOLOGICAL ANATOMY.—There are no characteristic lesions found after death. The lesions of typhoid fever are not present. Bruce has found in the spleen a micrococcus which has been called micrococcus Melitensis. This has been cultivated, and by it the disease has been reproduced in monkeys.

SYMPTOMS.—The period of incubation is about fourteen days.

The onset is gradual. There are malaise, headache, anorexia, and sleeplessness. These may last from one to four weeks. Then follows a period of improvement, during which the patient apparently enters upon convalescence. In a few days, however, the symptoms recur and with greater severity. The headache now is intense. There may be chills. The temperature is from 101° to 104° F. The temperature curve is very irregular. It may be remittent in type, or it may be intermittent, or it may resemble closely that of typhoid fever. The tongue is coated and moist. There is anorexia. There may be nausea and vomiting. In some cases there is diarrhœa. Sometimes there are cerebral symptoms, apathy, or delirium. Headache is generally well marked. After continuing from five to six weeks there is a remission of the above symptoms, and again the patient begins to convalesce. After from ten to twelve days there may again be a relapse. In many cases the remissions and relapses are less clearly marked. The disease shows a tendency to continue for from one to six months. There are generally very marked anæmia and debility. Late in the course of the disease there are commonly very severe neuralgic pains in the back and limbs. These are often the most pronounced features. There may be swelling of the joints. Convalescence when it sets in is often very slow, and in many cases two or three years elapse before the patient regains his normal good health. The death rate is about 2 per cent. The average stay in hospital is from seventy to eighty days.

The PROGNOSIS is fairly good. The mortality is about 2 per cent.

The TREATMENT consists of rest in bed and fluid diet, and in some cases quinine has been given in considerable doses.

MILIARY FEVER; SWEATING FEVER.

DEFINITION.—An infectious disease occurring in epidemics of varying intensity and duration. The disease was first described in 1485 in London, where a severe epidemic occurred in that year. It was called *sudor Anglicus.* In this outbreak it was characterized by symptoms of great severity, and a large proportion of the cases were fatal. It occurred several times in the seventeenth century in France and Germany. In 1887 a severe epidemic of the disease took place in France in the department of Vienne.

ETIOLOGY.—The etiology of the disease is unknown. It is supposed to be due to a micro-organism. The period of incubation is variable, and may be very short, less than twenty-four hours. Susceptibility is universal, and is the same for all ages and both sexes. One attack does not produce future immunity.

SYMPTOMS.—The attacks generally begin with acute gastric distress and a sense of lassitude. These in some cases precede the appearance of the other symptoms by several days. Generally, however, in the night following the onset of these prodromata the patient is awakened by a profuse perspiration.

In the early stages there are fever, sweating, great debility, and a variety of nervous symptoms. There is often paroxysmal dyspnœa, with no discoverable lesion of the lungs. There may be a sense of constriction in the epigastrium. Sometimes there are restlessness and delirium. There may be muscular cramps. The tongue is coated, the appetite is absent, and the bowels are constipated. Later, there is generally cough, and in some cases epistaxis, which is sometimes profuse.

An eruption generally appears on the fourth day, and with this the other symptoms are apt to become less marked. The eruption itself consists of a rash which may be in crescentic patches, resembling that of measles, or may be diffuse and like that of scarlatina, or it may be purpuric. But in each case there is superimposed upon it the miliary eruption proper, consisting of numerous miliary papules which gradually change to vesicles that then discharge and desquamate.

As the eruption becomes more marked the sweating diminishes, the temperature falls, and the debility and headache become less. At this time the cough commonly becomes more frequent, and bronchial râles are heard on auscultation. Constipation persists. The urine is diminished, but contains no albumin. In some cases there are hæmoptyses. In a few cases intestinal hemorrhage occurred.

Next following comes the stage of desquamation. Convalescence begins on the ninth or tenth day, and generally proceeds slowly. It is marked by great prostration and anæmia, and is often much prolonged.

Cases of miliary fever differ much in their severity. Sometimes the patient is not ill enough to have to go to bed. In other cases the disease begins suddenly and with great severity, and is rapidly fatal. Anomalous forms of the disease are described in which the eruption and sweating are wanting.

The PROGNOSIS depends probably upon the character of the epidemic. In some epidemics the death rate is very high.

The TREATMENT is entirely symptomatic.

SIMPLE CONTINUED FEVER.

DEFINITION.—From time to time cases of disease are met with in which an elevation of the temperature is the only symptom or is the most prominent symptom, and which do not admit of being classed with any of the well recognized diseases. It has become the habit of many observers to group these cases together under the name simple continued fever, and to assume that they represent a specific disease of unknown causation, but admitting of classification upon a purely clinical basis. Hence in medical literature are found a number of descriptions, in more or less detail, of a disease variously called simple continued fever, febricula, ephemeral fever, or catarrhal fever. Clinical study of the cases thus named and of the literature of the subject discloses the fact that they are far from uniform in their manifestations, and brings the conviction that so-called simple continued fever in most cases is not a specific disease, but is a group of clinical phenomena comprising irregular cases of many different maladies.

ETIOLOGY.—Many of the cases thus described are typhoid fever of mild or abortive type; others are ptomaïne-poisoning from the intestine; others are cases of mild tuberculosis where the tubercular focus is not to be found by clinical investigation.

Then there are the many kinds of poisoning by the streptococcus pyogenes, where the local symptoms may be so little marked that they are entirely overshadowed and masked by the general symptoms. This is especially apt to occur in a streptococcus inflammation of the throat, where sometimes the local trouble may be entirely unnoticed by the patient, and may be discovered only by a searching examination of the fauces. These cases sometimes present the clinical picture of so-called simple continued fever.

Leaving out of consideration all of the above mentioned cases, there are left remaining a considerable number of instances of continued fever whose causation cannot be explained. These cases, however, vary so much in their mode of onset, their duration, and their associated conditions that it is impossible to regard them as one and the same disease. For clinical purposes they may be divided into three groups, according to their duration:

First, those of short duration, lasting only a few days;

Second, those of moderately long duration, from one to three weeks;

Third, those of long duration, lasting for many weeks or months.

SYMPTOMS.—The first set of cases is very often met with, especially in hospital practice. The patients complain of lassitude, sometimes of headache. The temperature is from 100° to 102° F. The pulse is moderately rapid, 80 to 90. The symptoms regularly subside in from two to five or six days if the patient remains in bed.

Many of these cases, especially as met with in hospitals, are apparently due to fatigue or exposure—some to exposure to heat, but not severe enough to give rise to sunstroke. This moderate disturbance of the heat-regulating function of the body seems capable of being brought about by a large variety of causes. These cases require only rest in bed and good nursing.

The second set of cases, those of longer duration, are less often seen. In these the onset is gradual. The patient complains of malaise and headache. The tongue is coated. The bowels may be moderately constipated. The temperature is slightly elevated in the morning, 99.5° to 100.5° F. It is from one to two degrees higher in the afternoon. The e is somewhat more rapid than normal. The spleen is not enlarged. ere is no eruption. The examination of the blood is normal. The isease lasts for from one to three weeks or sometimes longer, and the nptoms disappear gradually. At no time is the patient very ill. The rse of the disease is not influenced by quinine.

The nature of these cases is obscure. Some of them may be cases of very mild typhoid fever. In many epidemics of typhoid, cases of mild fever like the above are met with, or they may be cases of infec-ion with the poison of influenza. It is believed by some observers iat they form a specific disease produced by a special poison, probably micro-organism.

The cases of the third variety, those of long duration, seem to epend upon locality. They have been described by Delafield as occur-ng in New York City. ents feel tolerably well in the morn-g, at which time the tem is normal or it may be slightly ove normal. In the after re are lassitude and slight headache. he pulse is moderately The temperature is from 100° to 01° F., or it may be a littl ner. There is no marked loss of weight nor of strength. The pati regularly go about their usual occupations, but feeling always ne fectly well. The tongue may be coated, nd there may be some dys nd constipation. The disease is not ffected by quinine or other m ation.

The duration is inde symptoms generally continue until e patient is removed climate.

The nature of the di irely unknown. It is often supposed be malarial, but there on for supposing that it is due to the alarial poison. It has als n ascribed to sewer-gas poisoning and to chronic poisoning by arsenic, as from wall paper.

The only TREATMENT that avails is the removal of the patient from the place where he acquired the disease.

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